Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Iniciativa científica de:
GECP lung cancer research

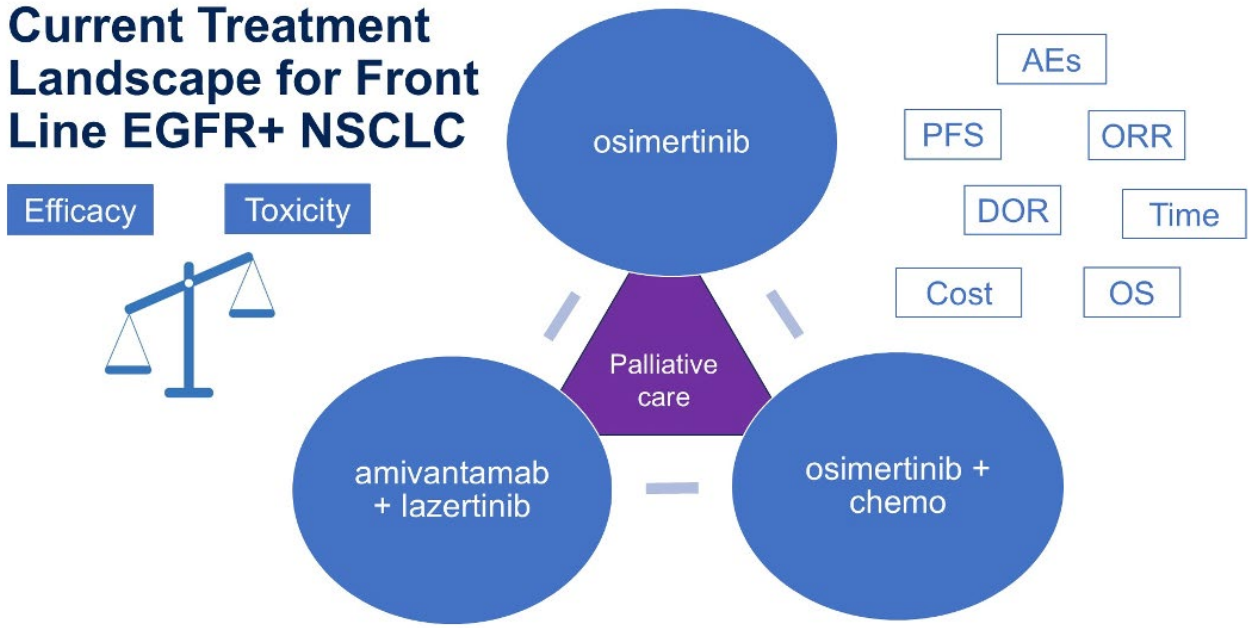
Enfermedad avanzada dirigidos a diana. Conclusiones

Mónica Antoñanzas Basa

Hospital Clínico San Carlos

EGFR

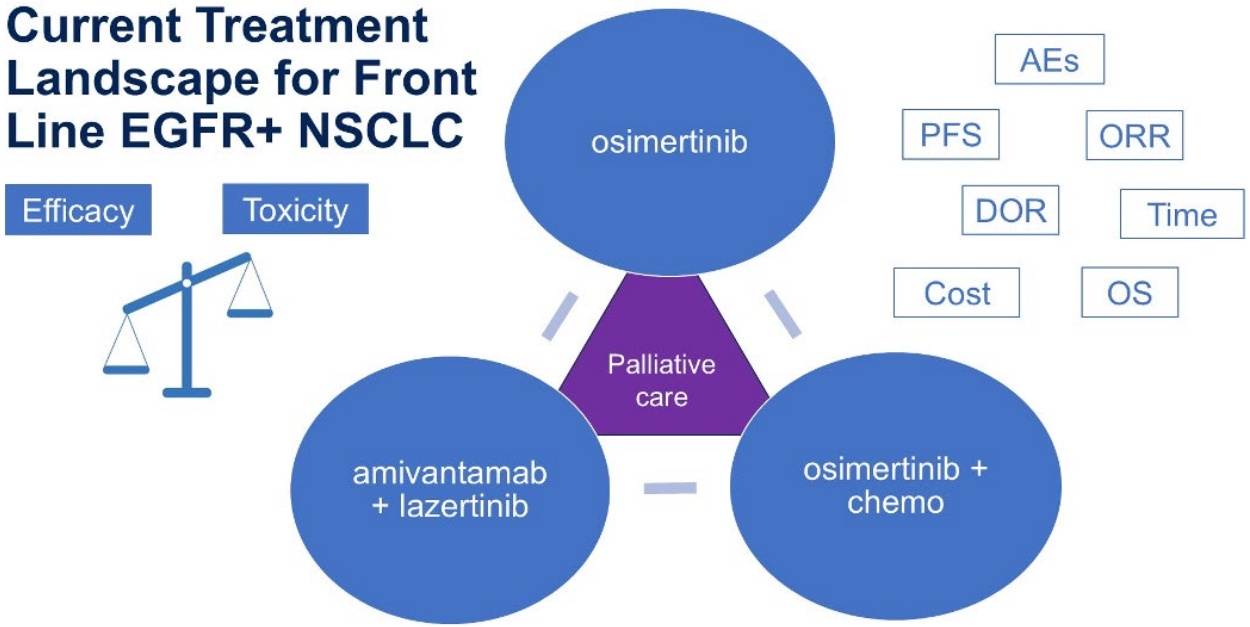
Decision



Baumann ASCO 2025

EGFR

Decision



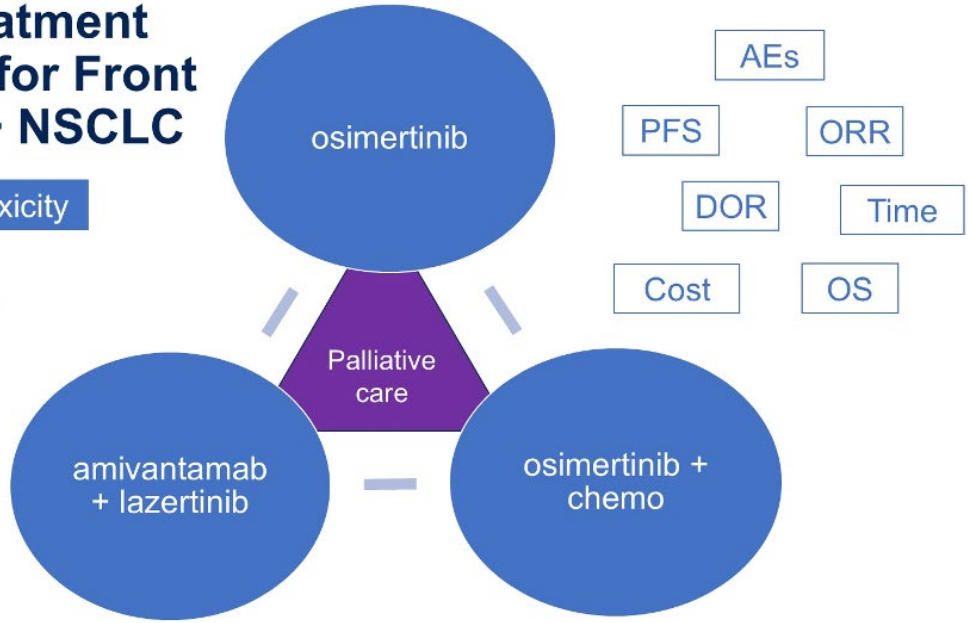
Baumann ASCO 2025

EGFR

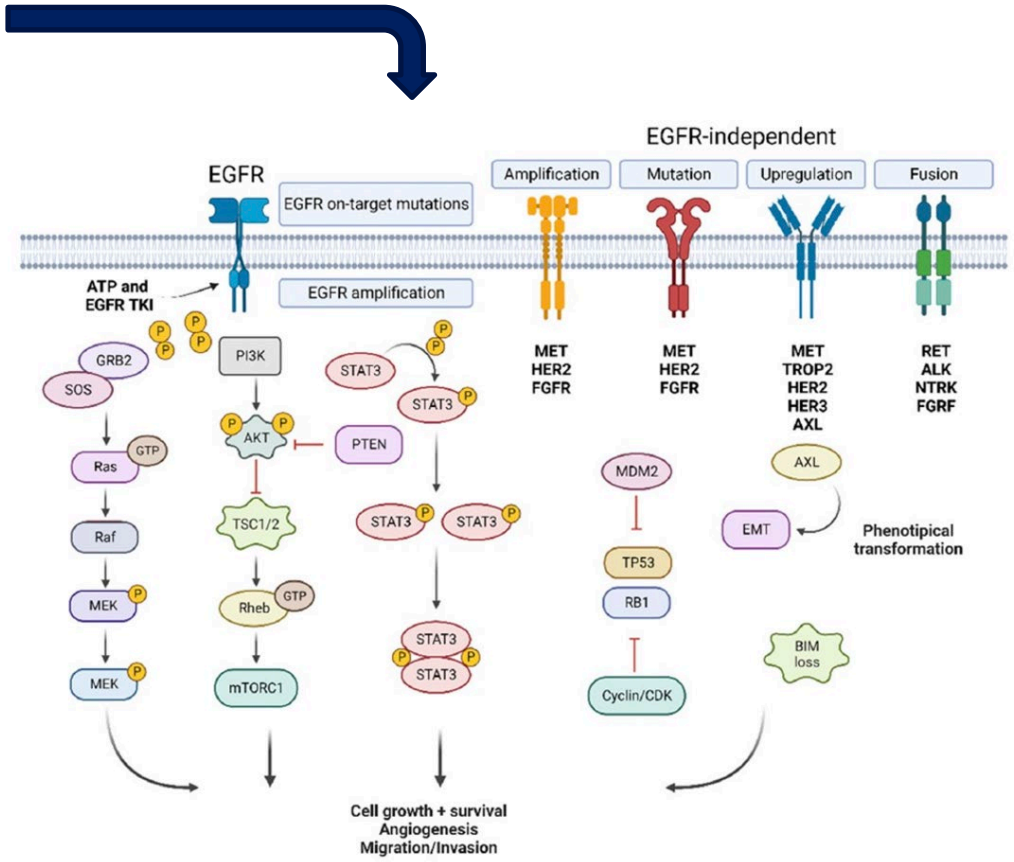
Decision

Current Treatment Landscape for Front Line EGFR+ NSCLC

Efficacy Toxicity



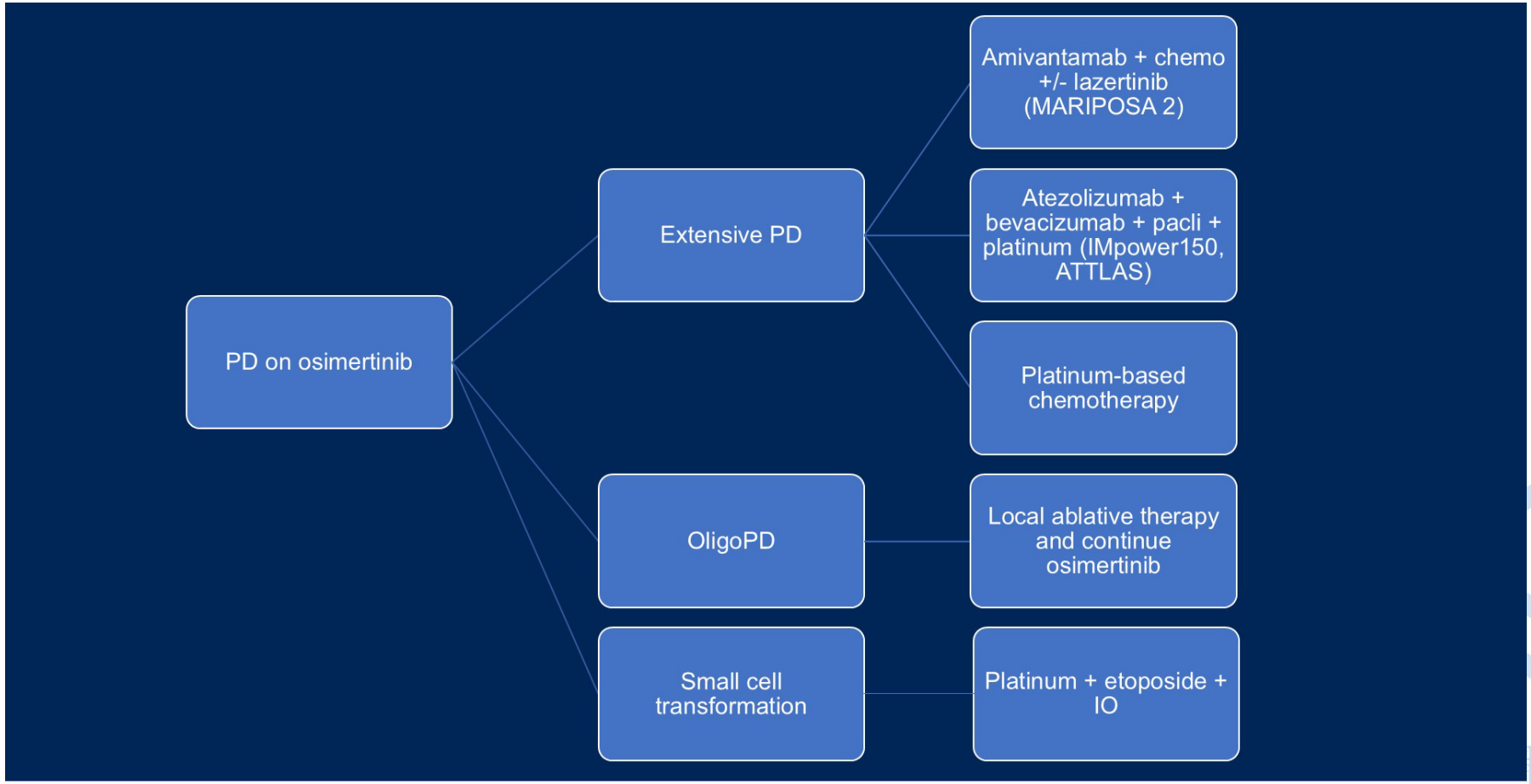
AEs
PFS
ORR
DOR
Time
Cost
OS



Baumann ASCO 2025

EGFR

Tratamiento a la progresion



EGFR. 2º línea MET

Oral Abstract 8505. SACHI study. Phase 3 Savolitinib + Osimertinib vs Chemo in MET amplified

- Unresectable or metastatic NSCLC
- EGFRm, PD on first-line EGFR-TKI
  - ➢ 1st /2nd G: T790M-, METamp;
  - ➢ 3rd G: METamp
- METamp (FISH+) confirmed by central lab
- ECOG PS 0-1

1:1

Savolitinib 600mg (BW≥50kg), or 400mg (BW<50kg) QD + Osimertinib 80mg QD
N = 106

→ **Until PD or intolerable toxicity**

Platinum +Pemetrexed 4~6 cycle then Pemetrexed maintenance
N = 105

→ **Until PD or intolerable toxicity**

→ **Conditionally crossovered to Savo-Osi after IRC-assessed PD**

METamp:

- **Post 1st /2nd G:** MET copy number ≥5 or MET/CEP7 ≥2
- **Post 3rd G:** MET copy number ≥ 10

Stratification factors:

- **Brain metastasis**: (yes or no)
- **Prior 3rd G EGFR-TKI**: (yes or no)
- **EGFR mutation**: (ex19del vs L858R vs others)

Primary endpoint: PFS by investigator

Secondary endpoints: PFS by IRC, ORR, DCR, DoR, TTR, OS, safety

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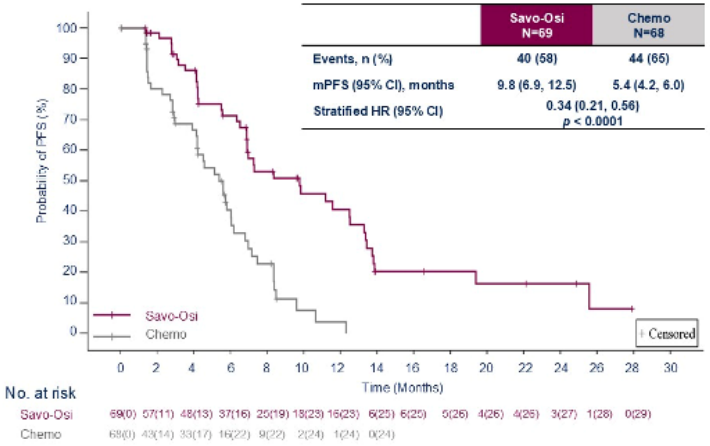
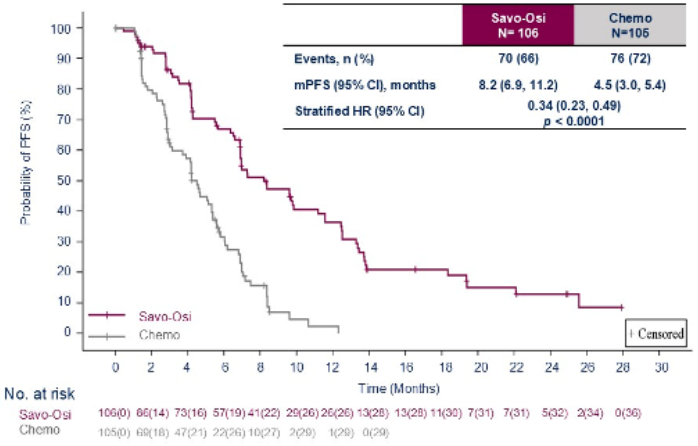
Progression-free Survival: Investigator

Prior 1st /2nd G EGFR-TKI-treated population



	Savo-Osi N=69	Chemo N=68
Events, n (%)	40 (58)	44 (65)
mPFS (95% CI), months	9.8 (6.9, 12.5)	5.4 (4.2, 6.0)
Stratified HR (95% CI)	0.34 (0.21, 0.56) $p < 0.0001$	

ITT population



	Savo-Osi N= 106	Chemo N=105
Events, n (%)	70 (66)	76 (72)
mPFS (95% CI), months	8.2 (6.9, 11.2)	4.5 (3.0, 5.4)
Stratified HR (95% CI)	0.34 (0.23, 0.49) $p < 0.0001$	

The predefined statistical significance thresholds for the primary endpoint were met in both the prior 1st /2nd G EGFR-TKI-treated and ITT populations.

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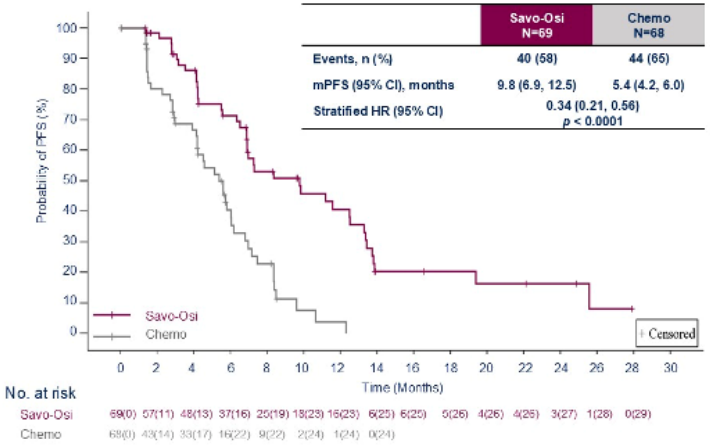

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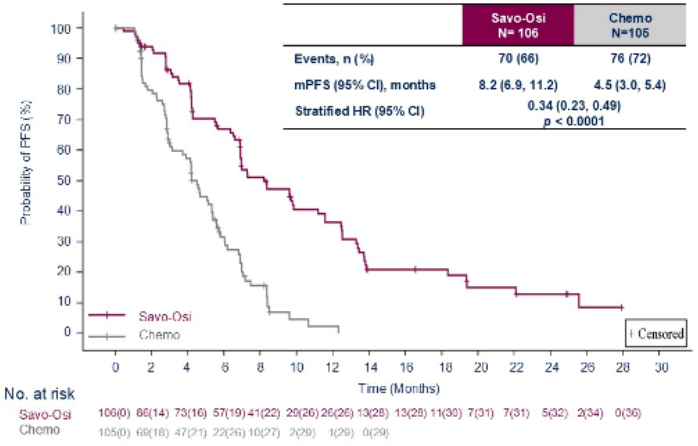
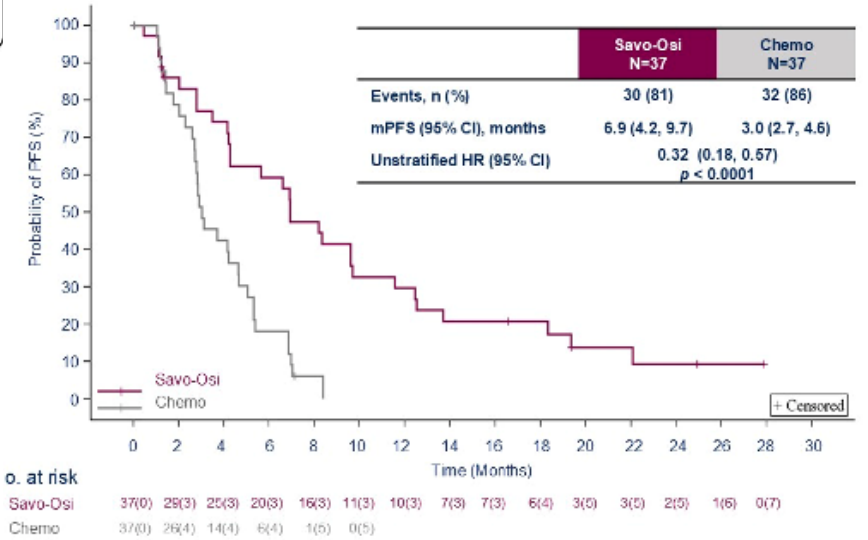


The predefined statistical significance thresholds for the primary endpoint were met in both the prior 1st /2nd G EGFR-TKI-treated and ITT populations.

- Prior 3rd G EGFR-TKI treated subgroup

Investigator

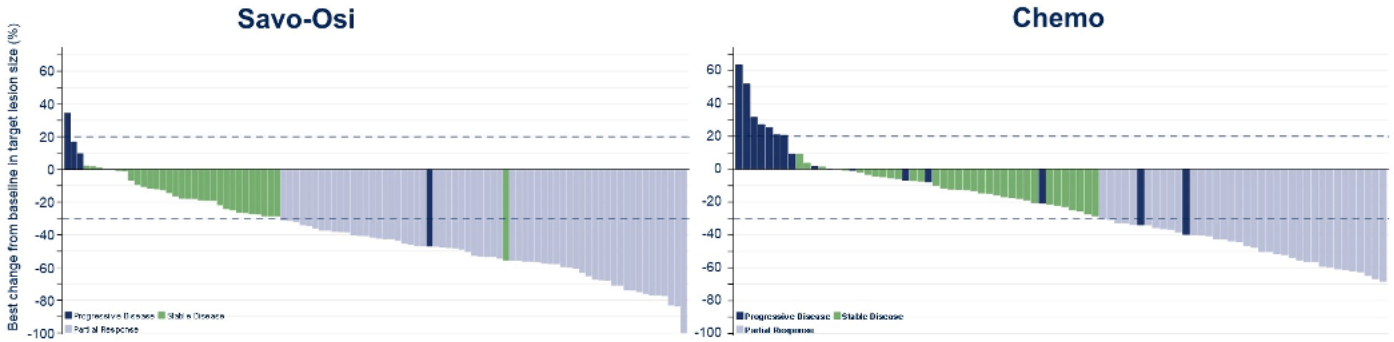
	Savo-Osi N=37	Chemo N=37
Events, n (%)	30 (81)	32 (86)
mPFS (95% CI), months	6.9 (4.2, 9.7)	3.0 (2.7, 4.6)
Unstratified HR (95% CI)	0.32 (0.18, 0.57) $p < 0.0001$	



EGFR. 2º línea MET

Oral Abstract 8505. SACHI study (China). Phase 3 Savolitinib + Osimertinib vs Chemo in MET amplified

ORR combination 58%



	Savo-Osi N=106	Chemo N=105	Stratified OR (95% CI)
ORR, % (95% CI)	58 (49-68)	34 (25-44)	2.74 (1.50-4.98) *p*=0.0004
DCR, % (95% CI)	89 (81-94)	67 (57-76)	3.98 (1.81-8.82) *p*=0.0001
Median DoR, month (95% CI)	8.4 (5.9-11.1)	3.2 (2.8-4.2)	-

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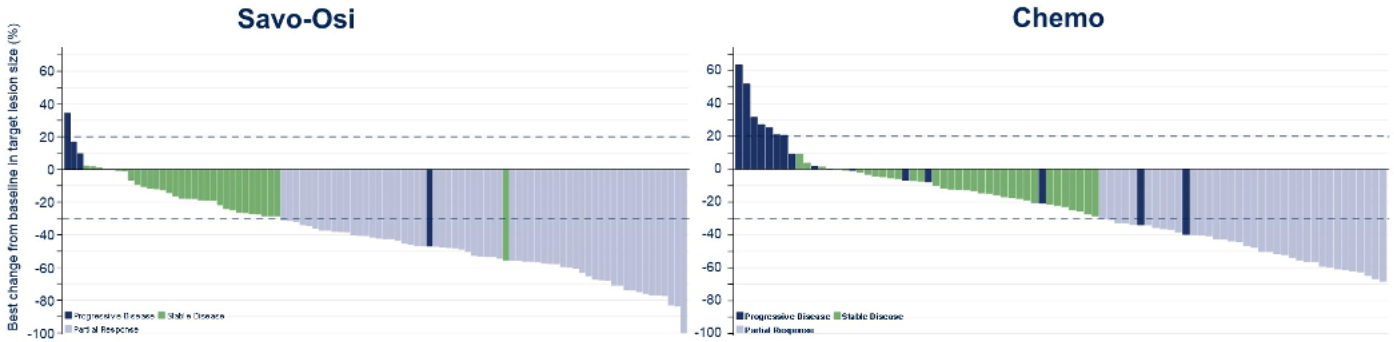

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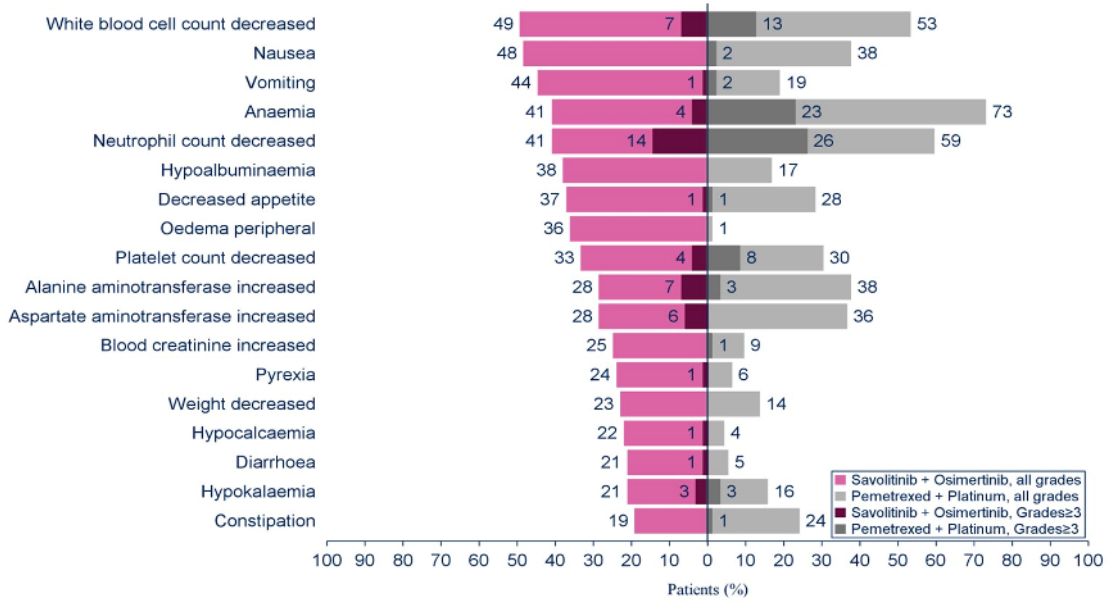

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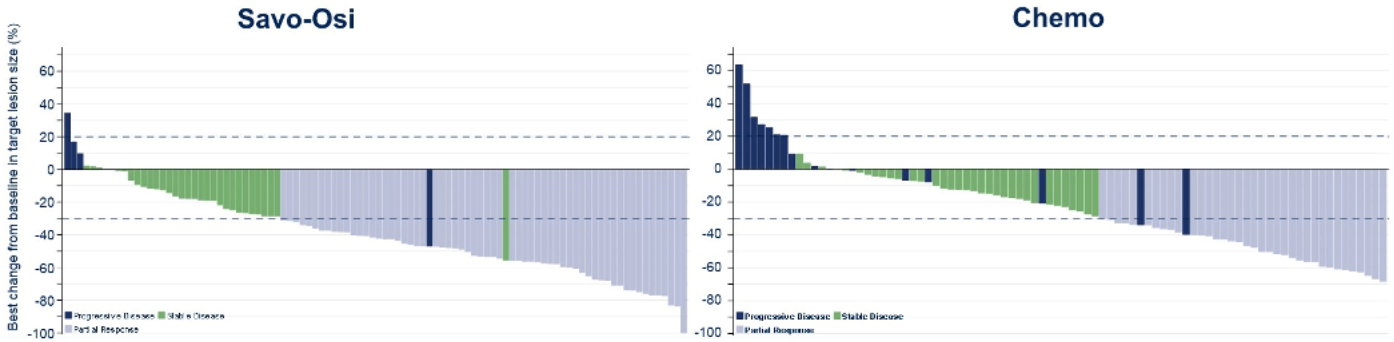

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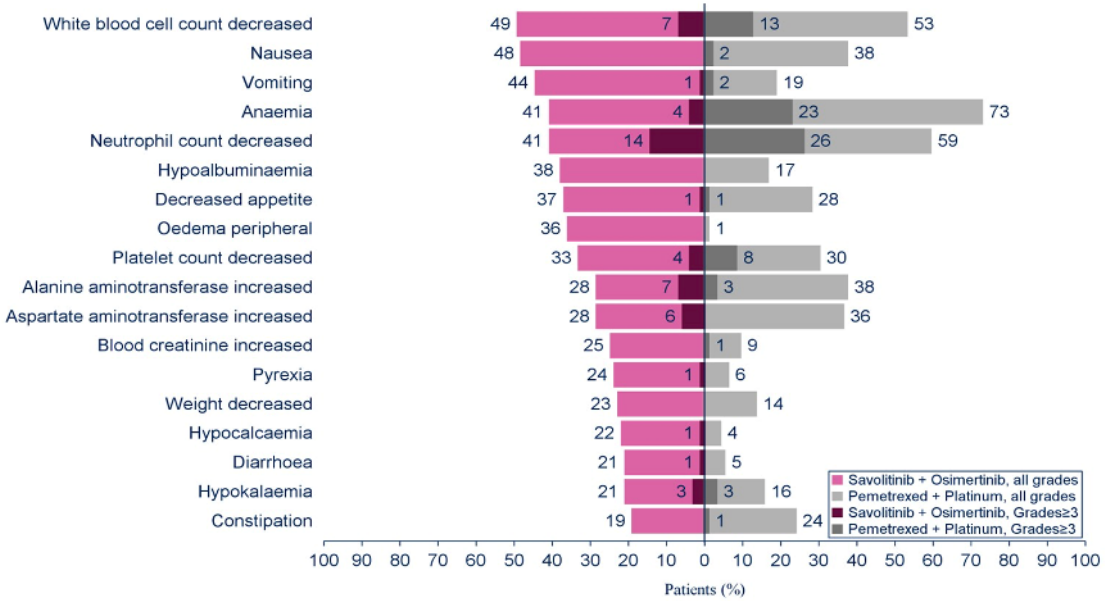

Efectos adversos gastrointestinales y edema periferico

EGFR. 2º línea MET

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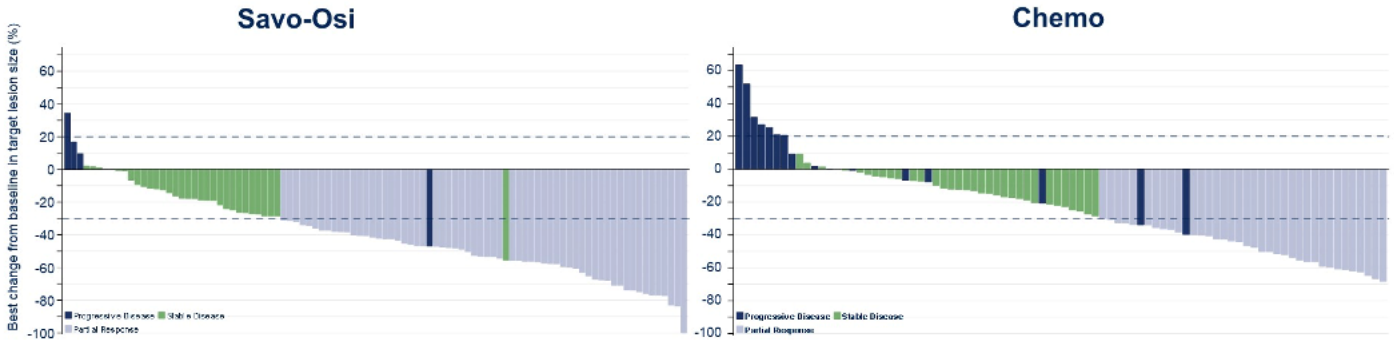

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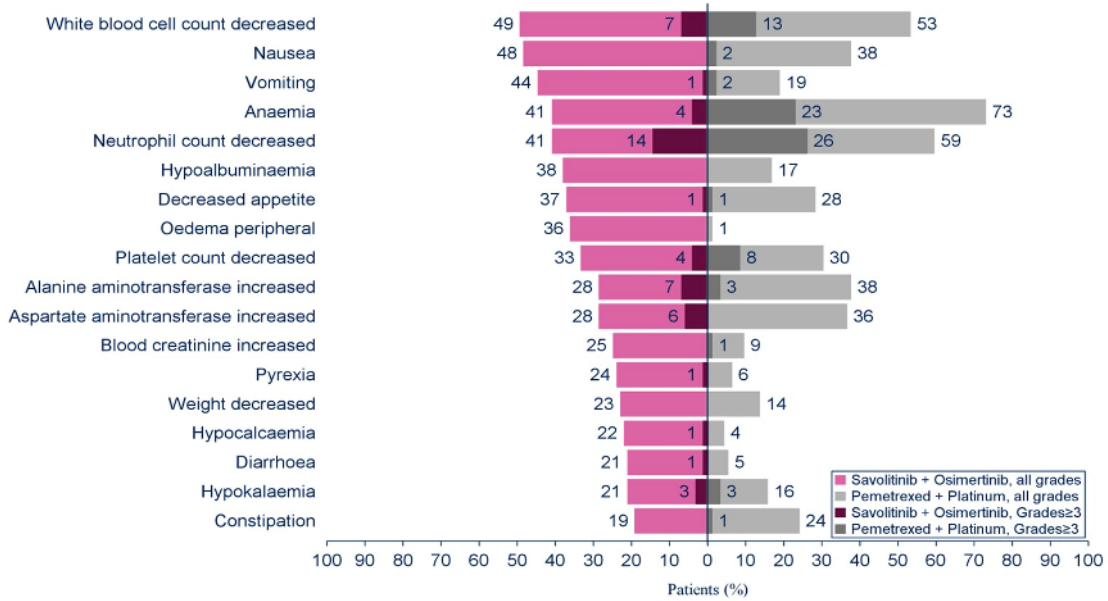
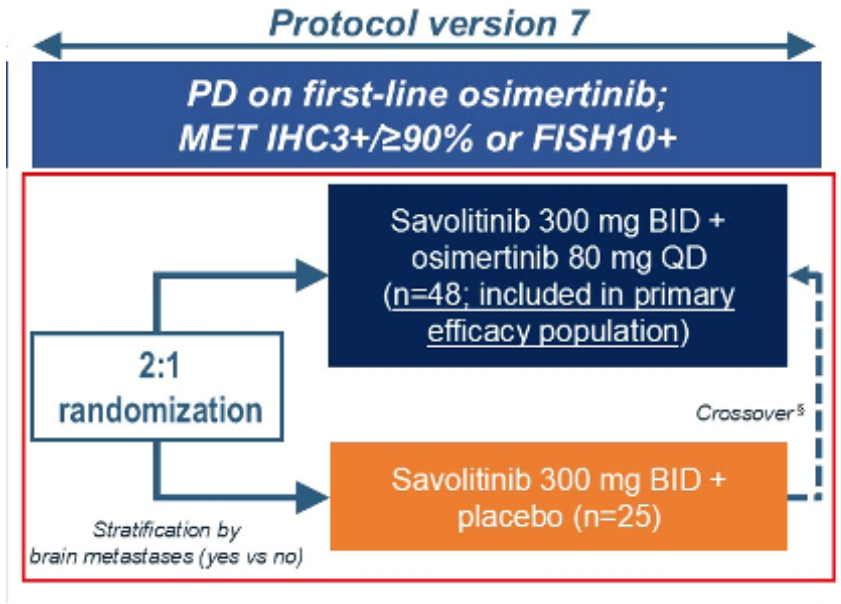


Efectos adversos gastrointestinales y edema periferico

	Savo- Osi N=106	Chemo N=105
Events, n (%)	39 (37)	45 (43)
mOS (95% CI), months	22.9 (16.8, NE)	17.7 (14.9, 26.3)
Unstratified HR (95% CI)	0.84 (0.55, 1.29)	

EGFR 2º línea MET

Rapid oral Abstract 8513. SAVANNAH . Phase II Osi + Savolitinib 300mg vs Savolitinib



	Population
Primary endpoint: ORR (investigator assessment)‖	MET IHC3+/≥90% and / or FISH10+ status after PD on first-line osimertinib (primary efficacy population; n=80)
	MET IHC3+/≥50% and / or FISH5+ status after PD on osimertinib

EGFR 2º línea MET

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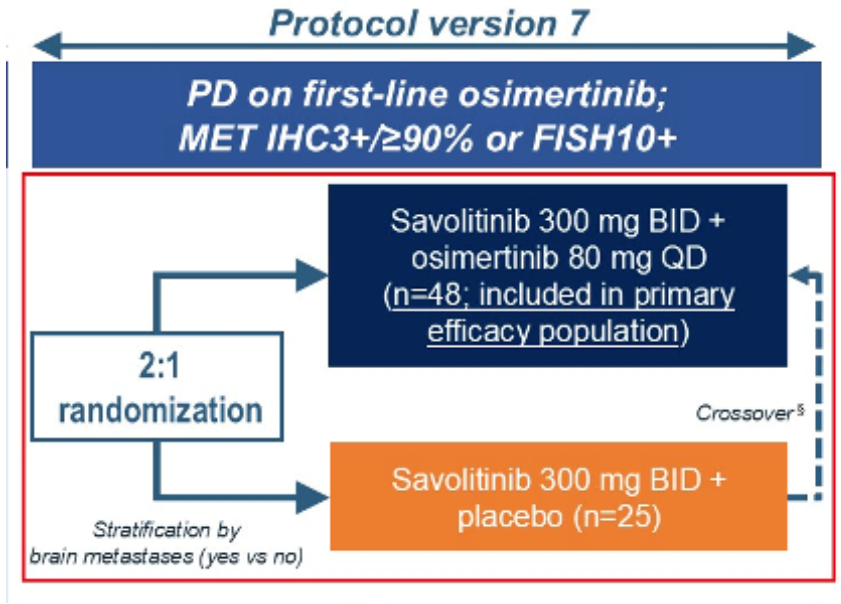
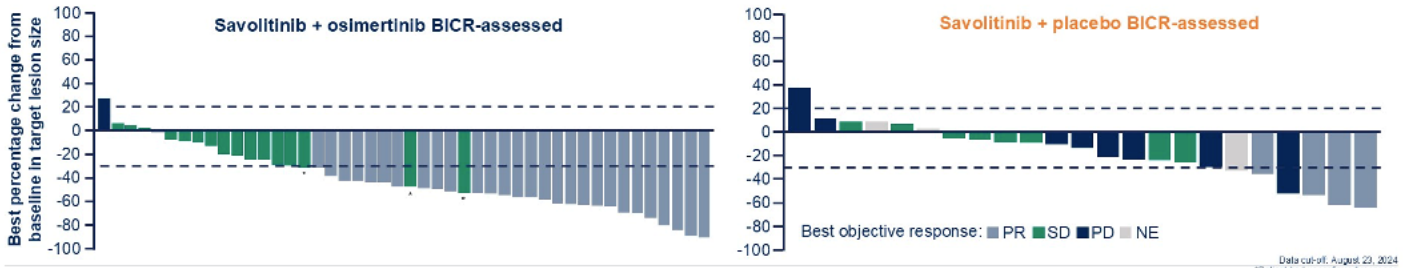


	Population
Primary endpoint: ORR (investigator assessment)‖	MET IHC3+/≥90% and / or FISH10+ status after PD on first-line osimertinib (primary efficacy population; n=80)
	MET IHC3+/≥50% and / or FISH5+ status after PD on osimertinib

- Confirmed ORR and median DoR were higher with savolitinib + osimertinib versus savolitinib + placebo; ORR and median DoR were similar when assessed by BICR or by investigator

	BICR-assessed		Investigator-assessed	
	Savolitinib + osimertinib (n=48)	Savolitinib + placebo (n=25)	Savolitinib + osimertinib (n=48)	Savolitinib + placebo (n=25)
Confirmed ORR, % (95% CI)	58 (43, 72)	16 (5, 36)	54 (39, 69)	24 (9, 45)
	(n=28)	(n=4)	(n=26)	(n=6)
Median DoR, months (95% CI)	11.8 (6.0, NC)	4.5 (2.6, NC)	8.0 (4.9, 11.7)	4.2 (2.6, NC)
Median time to onset of response, weeks (IQR)	6.0 (5.7–6.2)	6.1 (5.8–6.3)	6.1 (6.0–7.0)	6.1 (5.4–6.3)



EGFR 2º línea MET

Rapid oral Abstract 8513. SAVANNAH . Phase II Osi + Savolitinib 300mg vs Savolitinib

CNS efficacy by CNS BICR in patients with CNS metastases at baseline

- 14 patients in the savolitinib + osimertinib group and 4 patients in the savolitinib + placebo group had ≥1 measurable and / or non-measurable CNS lesion by CNS BICR at baseline

	Savolitinib + osimertinib (n=14)	Savolitinib + placebo (n=4)
CNS best objective response, n (%)		
Response	**6 (43)**	**1 (25)**
Complete response	2 (14)	0
Partial response	4 (29)	1 (25)
Non-response	**8 (57)**	**3 (75)**
Stable disease	7 (50)	1 (25)
Progressive disease	1 (7)	1 (25)
Not evaluable	0	1 (25)
CNS confirmed ORR, % (95% CI)	43 (18, 71)	25 (1, 81)
CNS median DoR, months, (95% CI)*	NR (6.0, NC)	6.9 (NC, NC)
CNS PFS events, n (%)	5 (36)	2 (50)
Median follow up for CNS PFS, months (95% CI)	5.8 (1.6, 16.6)	2.1 (0.0, 8.5)

EGFR 2º línea MET

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Median PFS, months (95% CI)

Savolitinib + osimertinib	8.3 (5.8, 15.1)
Savolitinib + placebo	3.6 (1.4, 5.7)

PFS HR (95% CI): 0.27 (0.13, 0.57)

PFS events / patients
Savolitinib + osimertinib 26 / 48 (54% maturity)
Savolitinib + placebo 14 / 25 (56% maturity)

EGFR 2º línea MET

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Median PFS, months (95% CI)

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PFS events / patients
Savolitinib + osimertinib 26 / 48 (54% maturity)
Savolitinib + placebo 14 / 25 (56% maturity)

Latest efficacy findings from SAVANNAH suggest that targeting both EGFR and MET alterations in MET-mediated resistance to osimertinib is key for systemic and intracranial activity and support further investigation of savolitinib + osimertinib, including CNS activity, in the Phase 3 SAFFRON study

EGFR. Savolitinib

Name	Design	N	Inclusion criteria	Endpoints	Results
SACHI	Phase 3 study of Osimertinib + savoltinib vs chemo	211	EGFRm, PD on 1st line EGFR TKI (65% 1st/2nd gen; 35% 3rd gen)	1º: PFS	ORR: 58% vs 34% mPFS: 8.2 vs 4.5; HR=0.34, P<0.0001 Grade≥3 AEs: 57% vs 57%
SAVANNAH	Phase 2 study of osimertinib + savolitinib	172	PD post 1-3 cycles of EGFR TKI, METamp (IHC 90%, FISH 10+)	1º: ORR	ORR: 55% mPFS: 7.5 mths (6.4-11.3) Grade≥3 AEs: 56.4%
ORCHARD	Phase 2 platform trial evaluating resistance to osi	30 (interim-20)	PD on 1L osimertinib with MET alterations on NGS	1º: ORR	ORR: 41% Grade≥3 AEs: 30%
SAFFRON	Phase 3 comparing osimertinib + savolitinib vs pem + carbo	324	Chemo naïve, PS 0-1, received osimertinib as 1st or 2nd line therapy	1º: PFS	NA
FLOWERS/CTONG2008	Ph 2 RCT comparing osi +/- savolitinib	44	Chemo naïve, EGFRm and METamp (IHC/NGS)	1º: ORR	ORR: 90.5% vs 60.9% mPFS: 19.6 vs 9.3; HR=0.8 (0.19-1.81); Gr≥3 AEs: 57.1% vs 8.7%
SANOVO	Ph 3 RCT savolitinib or placebo with osimertinib	320	First line EGFRm and METamp	1º: PFS	NA

Lu et al, ASCO 2025; Ahn M-J et al, ELCC 2025; Lu et al ESMO 2021; Oxnard et al, ASCO 2019; Lu et al, WCLC 2022; Yang WCLC 2024; Zhou et al, WCLC 2022

EGFR. 2º línea MET

Poster abstrat 8592. Furmonertinib + MET directed ADC RC108

Key inclusion criteria

- Histologically or cytologically confirmed Ia/m NSCLC
- EGFR sensitive mutation positive
- MET-overexpression defined as ≥IHC 1+ (≥10% of tumor cells has IHC 1+/2+/3+ staining in cytomembrane)
- Prior treatment with 1st/2nd/3rd-generation (G) EGFR-TKI
- At least one measurable lesion per RECIST v1.1

Study design

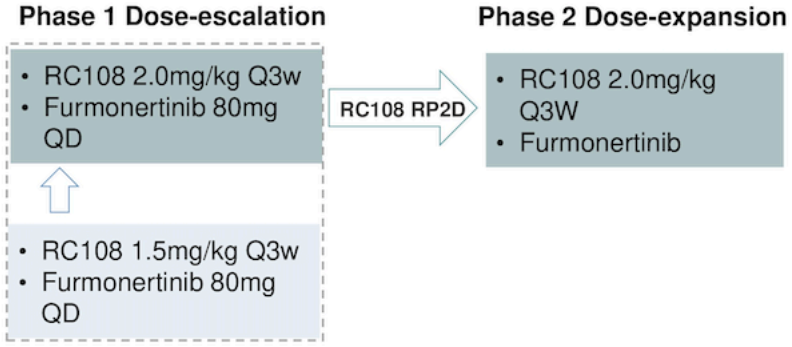
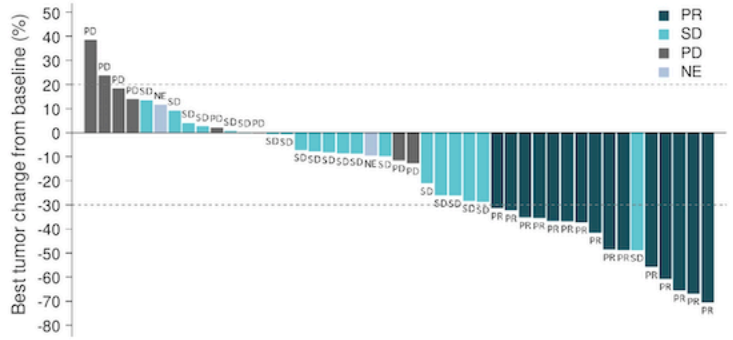


Table 3. Antitumor activity

	C-Met ≥ IHC 1+ (N = 45)	C-Met ≥ IHC 1+ and cytoplasmic 3+ ≤20% (N = 37)	C-Met ≥ IHC 3+ and cytoplasmic 3+ ≤20% (N = 18)
Best overall response, n (%)			
PR	15 (33.3)	15 (40.5)	11 (61.1)
SD	20 (44.4)	17 (45.9)	6 (33.3)
PD	8 (17.8)	4 (10.8)	1 (5.6)
NE	2 (4.4)	1 (2.7)	0
ORR, n (%)	15 (33.3)	15 (40.5)	11 (61.1)
DCR, n (%)	35 (77.8)	32 (86.5)	17 (94.4)

PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable.

Figure 1. Best overall tumor response



Safety

- Treatment-related adverse events (TRAEs) of any grade occurred in all patients, and grade ≥3 TRAEs in 17 (35.4%).
- TRAEs led to treatment discontinuation in 2 (4.2%) patients.

Table 3. TRAEs of any grade occurring in ≥20% patients

TRAEs^, n (%)	Any grade	Grade ≥3*
Asthenia	27 (56.3)	5 (10.4)
Nausea	23 (47.9)	2 (4.2)
Decreased appetite	21 (43.8)	0
Vomiting	21 (43.8)	2 (4.2)
Pain in extremity	19 (39.6)	0
Neutrophil count decreased	18 (37.5)	5 (10.4)
White blood cell count decreased	18 (37.5)	1 (2.1)
Hypoaesthesia	16 (33.3)	1 (2.1)
Alopecia	16 (33.3)	0
Weight decreased	14 (29.2)	0
Anaemia	13 (27.1)	1 (2.1)
Constipation	13 (27.1)	0
Aspartate aminotransferase increased	11 (22.9)	1 (2.1)
Myalgia	12 (25.0)	0
Pruritus	10 (20.8)	0

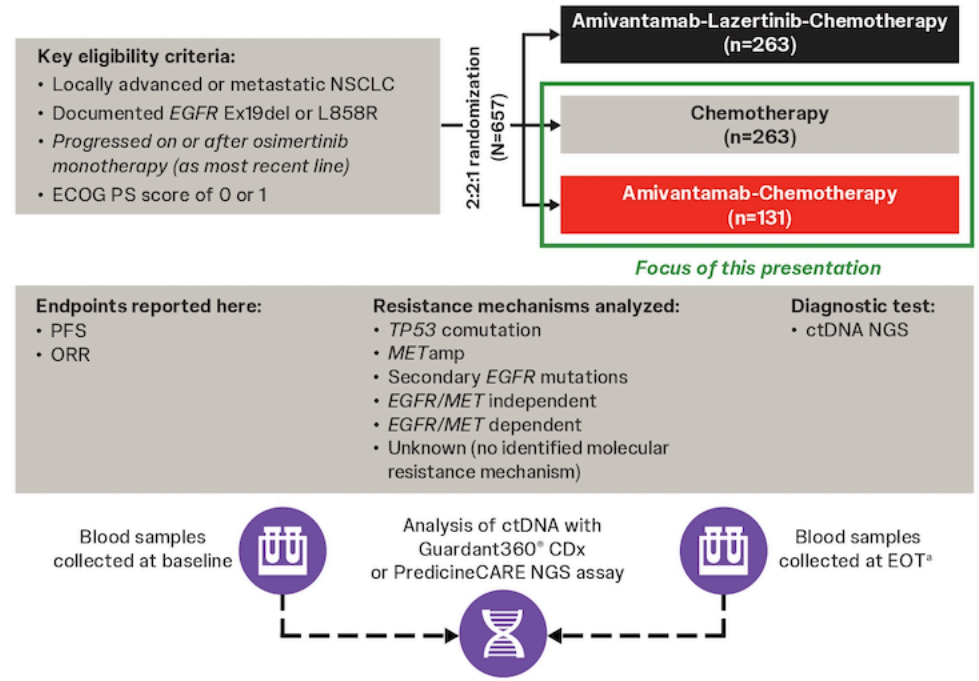
*Related to any study treatment. *Including two grade 5 events with abnormal hepatic function and death (unknown cause) occurring in one patient each.

Fase III en marcha

EGFR 2º linea

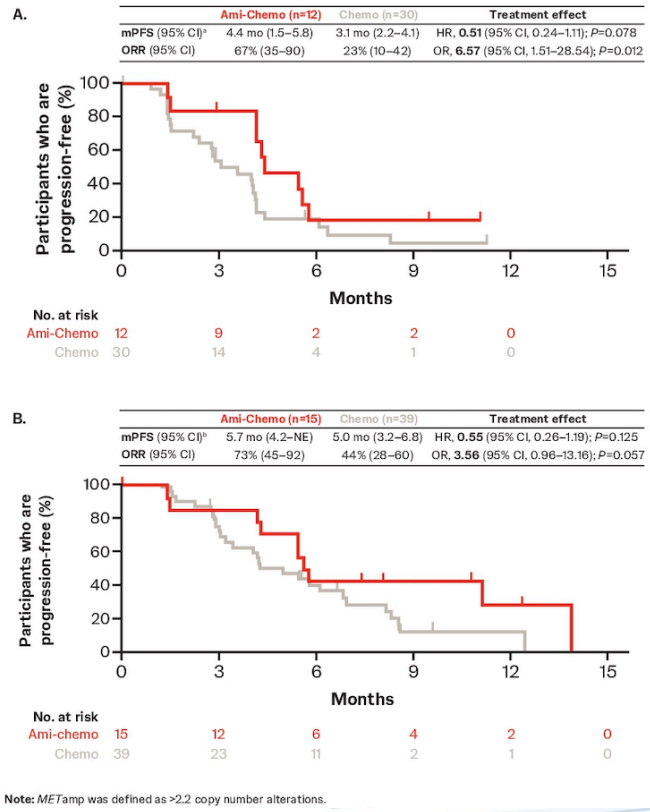
Poster Abstract. MARIPOSA 2. Outcomes by Osimertinib R

FIGURE 1: MARIPOSA-2 study design



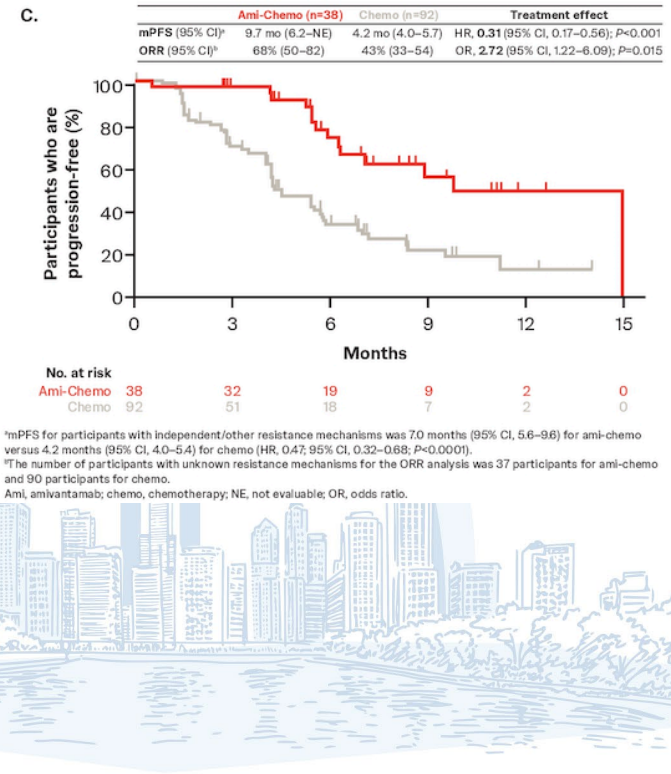
MARIPOSA-2 (ClinicalTrials.gov Identifier: NCT04988295); clinical cutoff: 10-Jul-2023.

FIGURE 5: Efficacy among participants with (A) *MET*amp and (B) secondary *EGFR* mutations



Note: *MET*amp was defined as >2.2 copy number alterations.

Unknown R mechanism

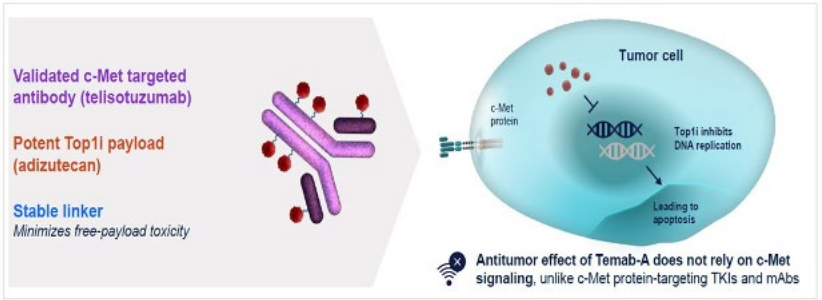


[a]mPFS for participants with independent/other resistance mechanisms was 7.0 months (95% CI, 5.6–9.6) for ami-chemo versus 4.2 months (95% CI, 4.0–5.4) for chemo (HR, 0.47; 95% CI, 0.32–0.68; P<0.0001).
[b]The number of participants with unknown resistance mechanisms for the ORR analysis was 37 participants for ami-chemo and 90 participants for chemo.
Ami, amivantamab; chemo, chemotherapy; NE, not evaluable; OR, odds ratio.

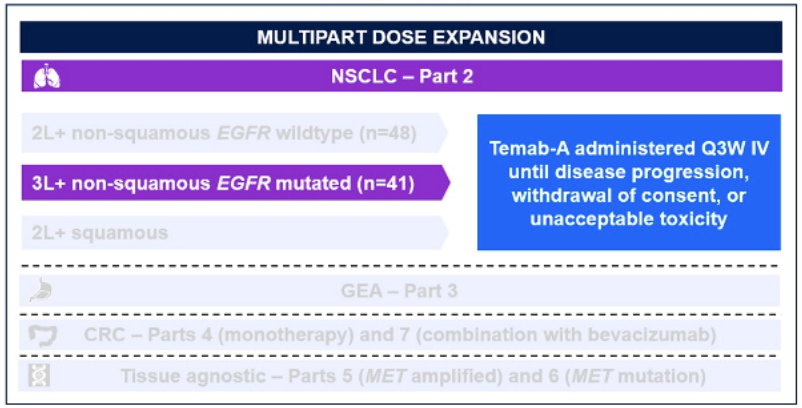
EGFR 3º línea

Rapid Oral Abstract 8512: Phase I Temab – A (Telisotuzumab – Adizutecan) MET antibody . All MET expresion

Temab-A Mechanism of Action[4]



Study Design



Primary objectives
- Evaluate safety, tolerability and PK of Temab-A
- Assess preliminary efficacy (ORR, CBR, DOR, PFS, OS)

Tumor tissue c-Met protein expression assessed centrally by IHC, using the clinical trial assay for MET (SP44) (Roche Diagnostics)

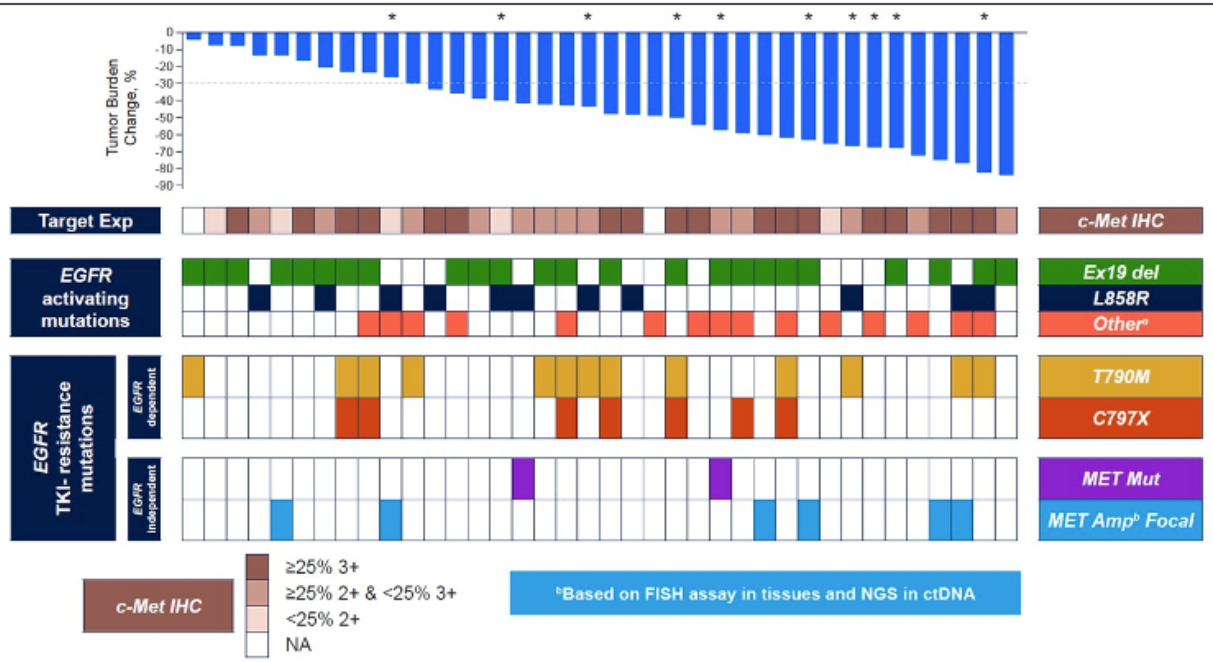
TEAEs, n (%)	*EGFR* MT NSCLC (N=41)	
	Any Grade	Grade ≥3
Any TEAE[a]	41 (100)	32 (78)
Gastrointestinal[b]	34 (83)	3 (7)
Hematological[b]	34 (83)	21 (51)
Anemia	26 (63)	13 (32)
Neutropenia	17 (41)	12 (29)
Non-hematological[b]		
Nausea	27 (66)	1 (2)
Vomiting	16 (39)	3 (7)
Decreased appetite	14 (34)	1 (2)
Fatigue	13 (13)	1 (2)
Constipation	13 (32)	-

EGFR 3º línea

Rapid Oral Abstract 8512: Temab- A MET antibody . All MET expresion

Outcome	Total (N=41)
Confirmed best overall response,[a] n (%)	
PR	26 (63)
SD	12 (29)
ORR,[b] n (%)	26 (63)
CBR,[c] n (%)	38 (93)
CBR12	34 (83)
CBR24	32 (78)
mDOR, mo	9.8 [8.3, 13.9]
mPFS, mo [95%CI]	10.9 [9.4, 12.3]
P[OS at 12 mo], % [95% CI]	69 [52, 81]

All patients with post-baseline data (n=38) experienced decrease in tumor burden



- Responses occurred irrespective of *EGFR* L858R alterations, exon 19 deletions or TKI resistance mutations, including T790M and C797S

Further studies

EGFR 3º línea

Rapid Oral Abstract 8512: Temab- A MET antibody . All MET expresion

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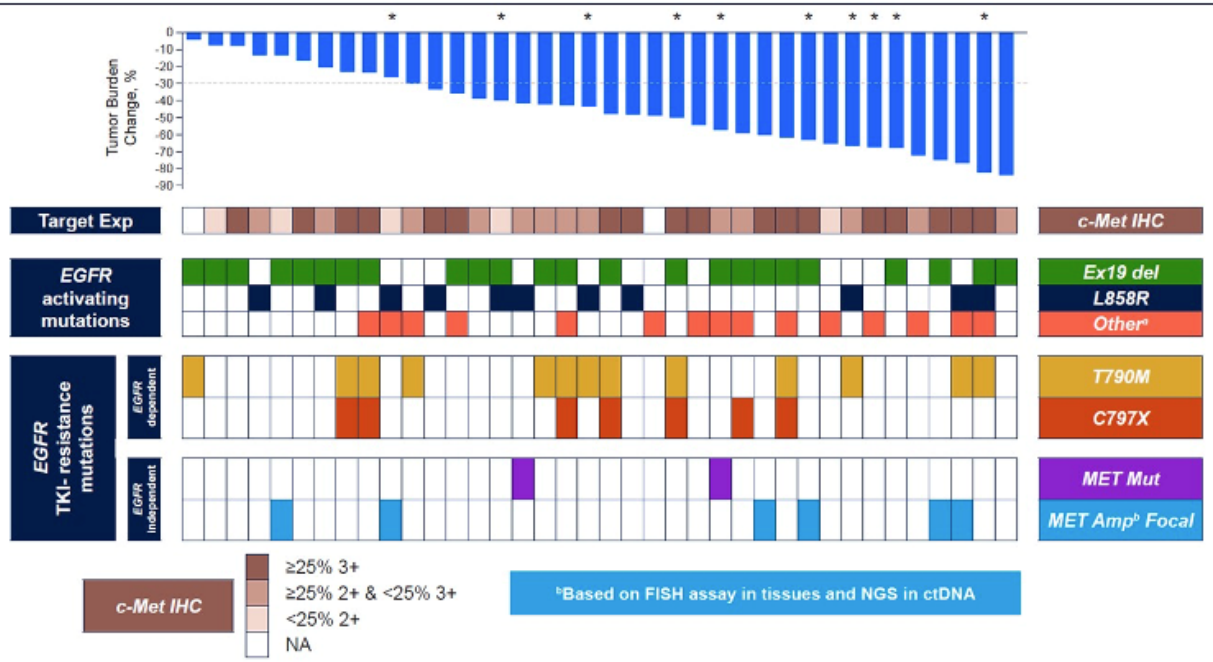

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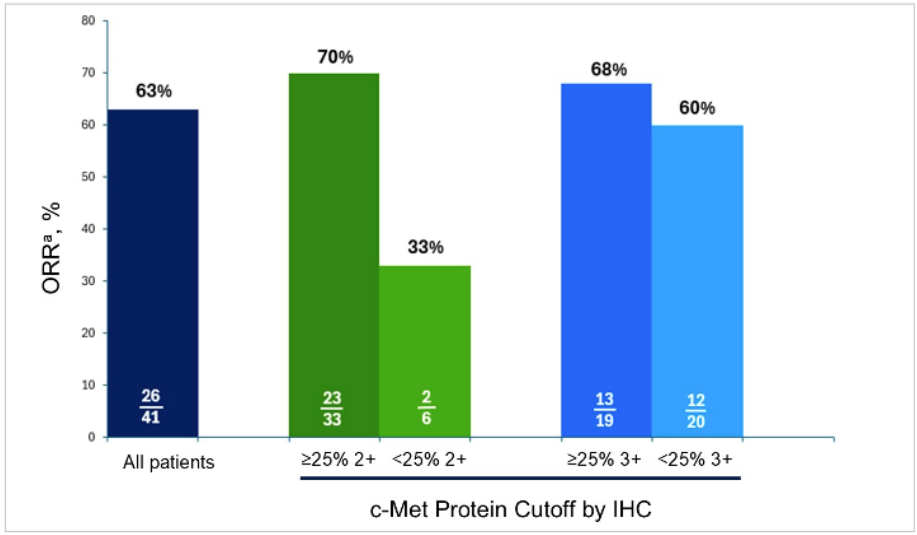
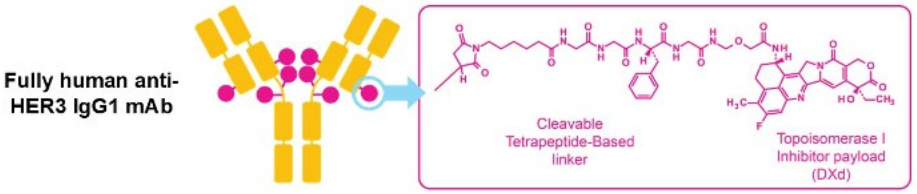
Further studies



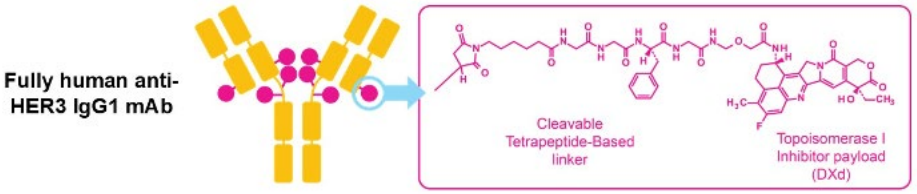
EGFR 2º linea

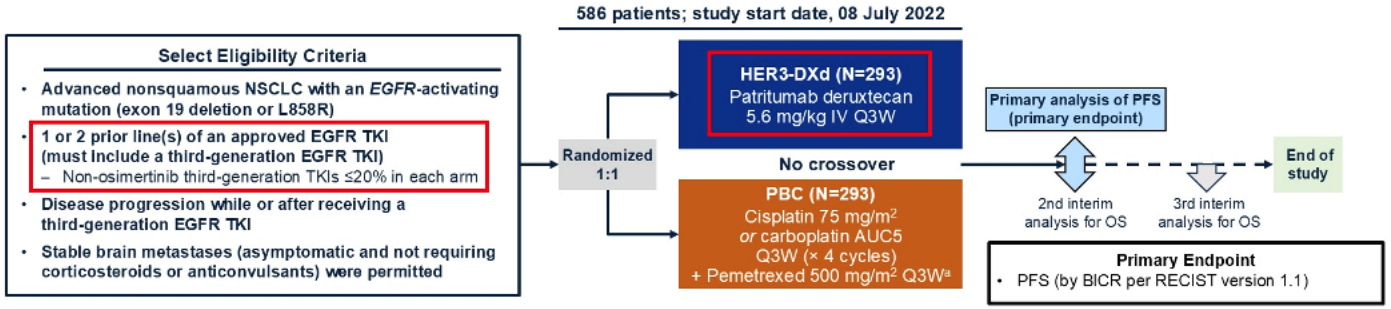
Oral Abstract HERTHENA Lung 02. Phase III Patritumab- DxD vs Chemo



EGFR 2º linea

Oral Abstract HERTHENA Lung 02. Phase III Patritumab- DxD vs Chemo





EGFR 2º linea

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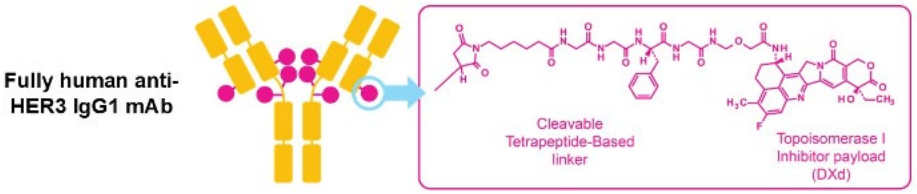
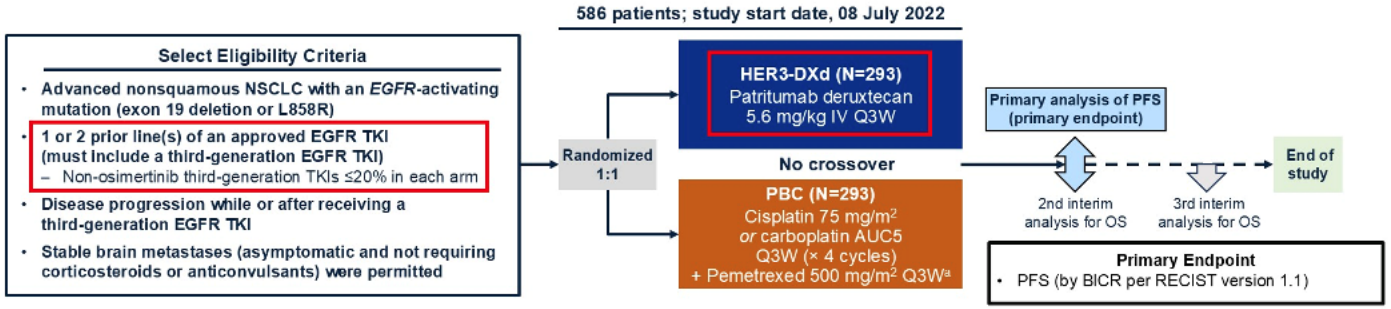
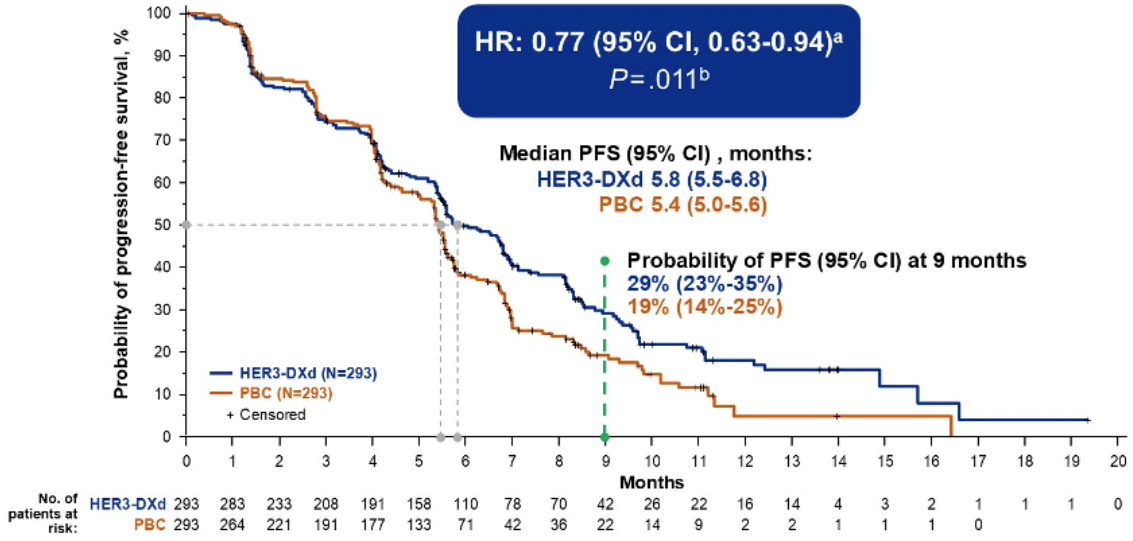


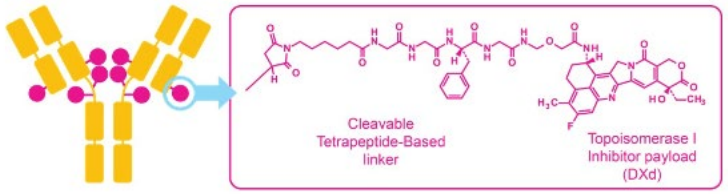


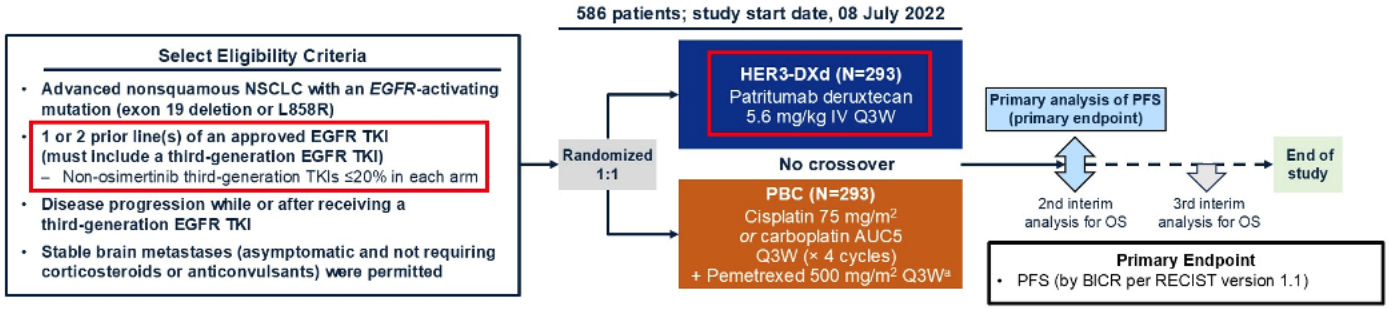
HER3-DXd significantly reduced the risk of disease progression (by BICR per RECIST 1.1) or death vs PBC



EGFR 2º linea

Oral Abstract HERTHENA Lung 02. Phase III Patritumab- DxD vs Chemo





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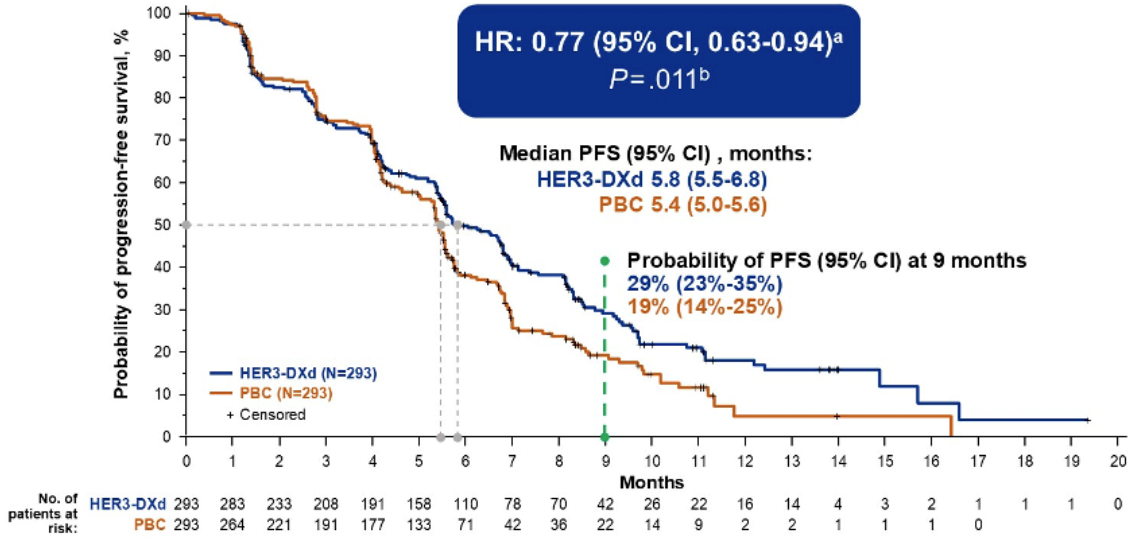
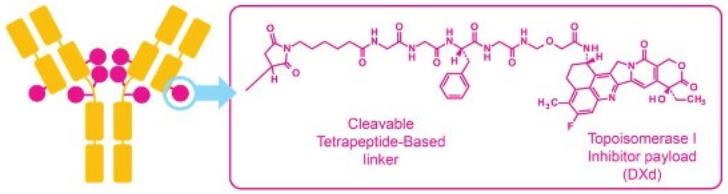


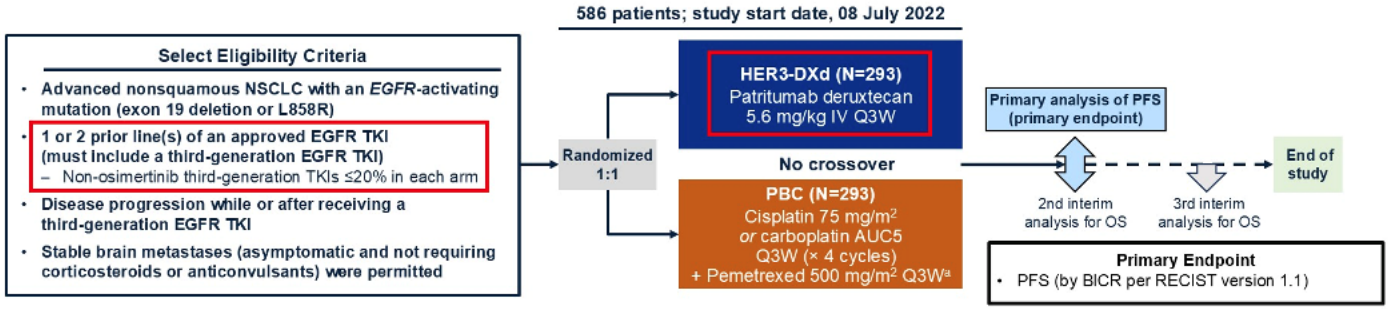
Responses by BICR per RECIST		HER3-DXd (N=293)	PBC (N=293)
Confirmed ORR (95% CI), %		**35.2 (29.7-40.9)**	**25.3 (20.4-30.6)**
Best overall response, n (%)	CR	1 (0.3)	3 (1.0)
	PR	102 (34.8)	71 (24.2)
	SD[a]	133 (45.4)	148 (50.5)
	PD	40 (13.7)	35 (11.9)
	NE	17 (5.8)[b]	36 (12.3)[c]
BOR to be confirmed, n (%)		2 (0.7)[d]	2 (0.7)[d]
DCR (95% CI), %		80.5 (75.5-84.9)	75.8 (70.4-80.6)
Median TTR (range), mo		1.5 (0.3-8.1)	1.5 (1.2-6.9)
Median DOR (95% CI), mo		5.7 (5.1-7.3)	5.4 (4.1-5.6)

Best change in SOD from baseline, %

EGFR 2º linea

Oral Abstract HERTHENA Lung 02. Phase III Patritumab- DxD vs Chemo





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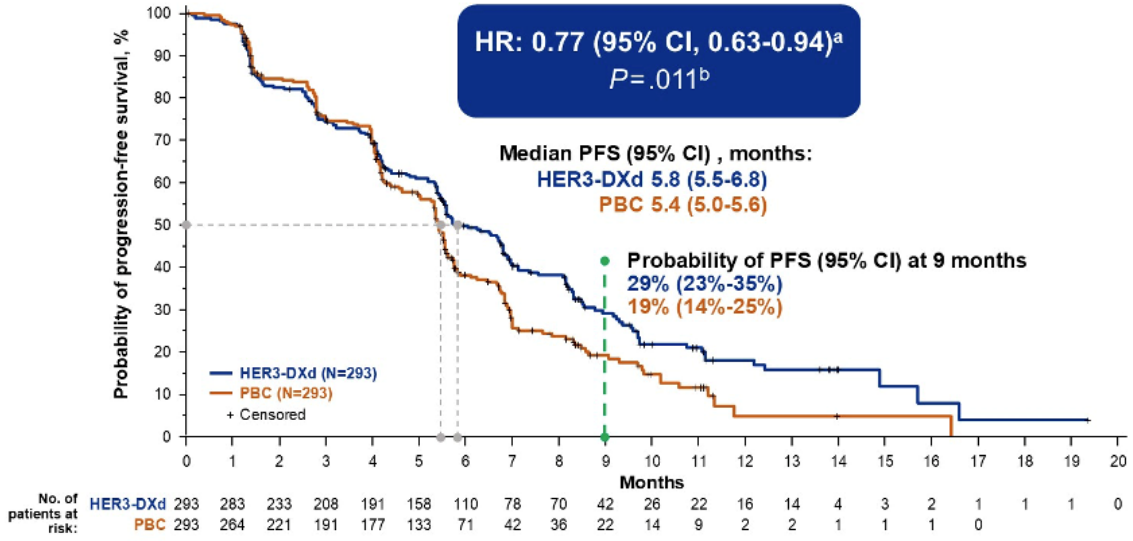

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Best change in SOD from baseline, %

No clinical benefit. Withdrawal petition to FDA

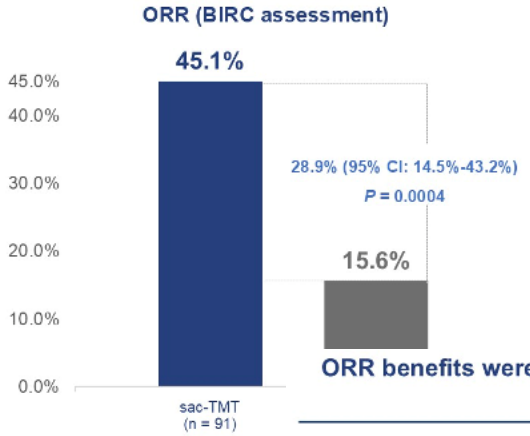
EGFR 3º Linea

Oral Abstract 8507. OptiTROP- 03. Sac- TMT vs Docetaxel (After Osi and platinum chemo)

Obejtivo: ORR. Crossover

Sac-TMT improved ORR with a statistically significant difference of 28.9% over docetaxel.

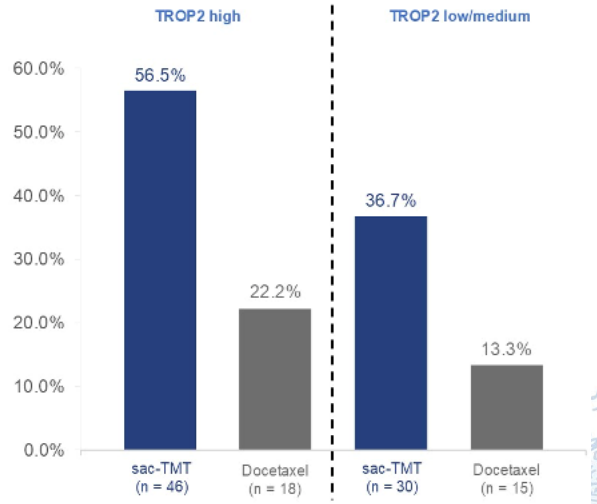
	Sac-TMT (n = 91)	Docetaxel (n = 45)
cORR, n (%) (95% CI)	41 (**45.1**) (34.6, 55.8)	7 (**15.6**) (6.5, 29.5)
Difference (95% CI)	**28.9 (14.5, 43.2)**	
One-sided P-value	0.0004	
DCR, n (%) (95% CI)	75 (82.4) (73.0, 89.6)	27 (60.0) (44.3, 74.3)
Difference (95% CI)	22.3 (6.0, 38.7)	
DOR, n (%)	26 (63.4)	6 (85.7)
Median DOR, months (95% CI)	**7.0** (5.4, 9.1)	**5.1** (3.1, NE)



- **ORR benefit favoring patients with sac-TMT over docetaxel across all pre-specified subgroups, including brain metastas**

ORR benefits were observed with sac-TMT over docetaxel regardless of TROP2 expression.

TROP2 Expression Levels	Sac-TMT (n = 76)	Docetaxel (n = 33)
TROP2 high, n (%)	46 (60.5)	18 (54.5)
cORR, n (%) (95% CI)	26 (**56.5**) (41.1, 71.1)	4 (**22.2**) (6.4, 47.6)
Difference (95% CI)	**34.3 (10.3, 58.3)**	
TROP2 low/medium, n (%)	30 (39.5)	15 (45.5)
cORR, n (%) (95% CI)	11 (**36.7**) (19.9, 56.1)	2 (**13.3**) (1.7, 40.5)
Difference (95% CI)	**23.3 (-1.0, 47.7)**	



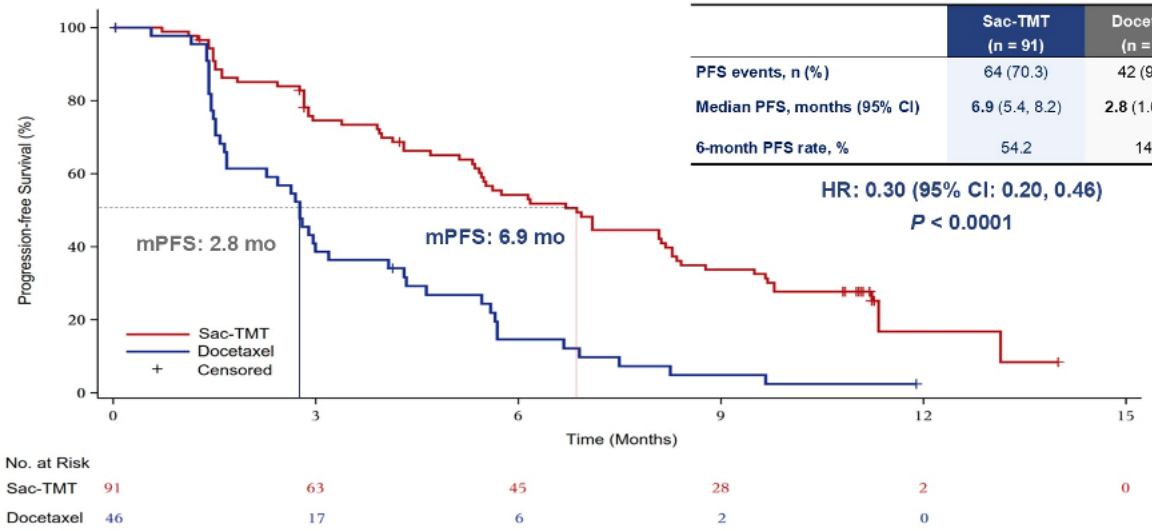
Data cutoff date: Dec 31, 2024.
TROP2 expression was assessed using IHC (monoclonal antibody: EPR20043) by MEDx Translational Medicine. **TROP2 high expression** was defined as **an IHC H-score >200**, and **TROP2 low/medium expression** was defined as an **IHC H-score ≤200.**

EGFR 3º Linea

Oral Abstract 8507. OptiTROP- 03. Sac- TMT (antiTROP2) vs Docetaxel

Obejtivo: ORR. Crossover

Sac-TMT significantly improved PFS over docetaxel with 70% lower risk of disease progression or death.



	Sac-TMT (n = 91)	Docetaxel (n = 46)
PFS events, n (%)	64 (70.3)	42 (91.3)
Median PFS, months (95% CI)	**6.9** (5.4, 8.2)	**2.8** (1.6, 4.1)
6-month PFS rate, %	54.2	14.6

HR: 0.30 (95% CI: 0.20, 0.46)

***P* < 0.0001**

EGFR 3º Linea

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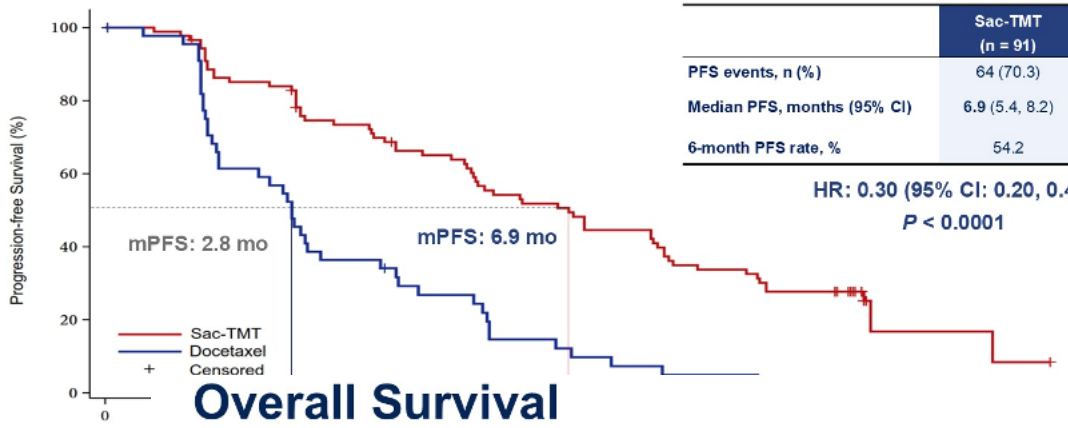

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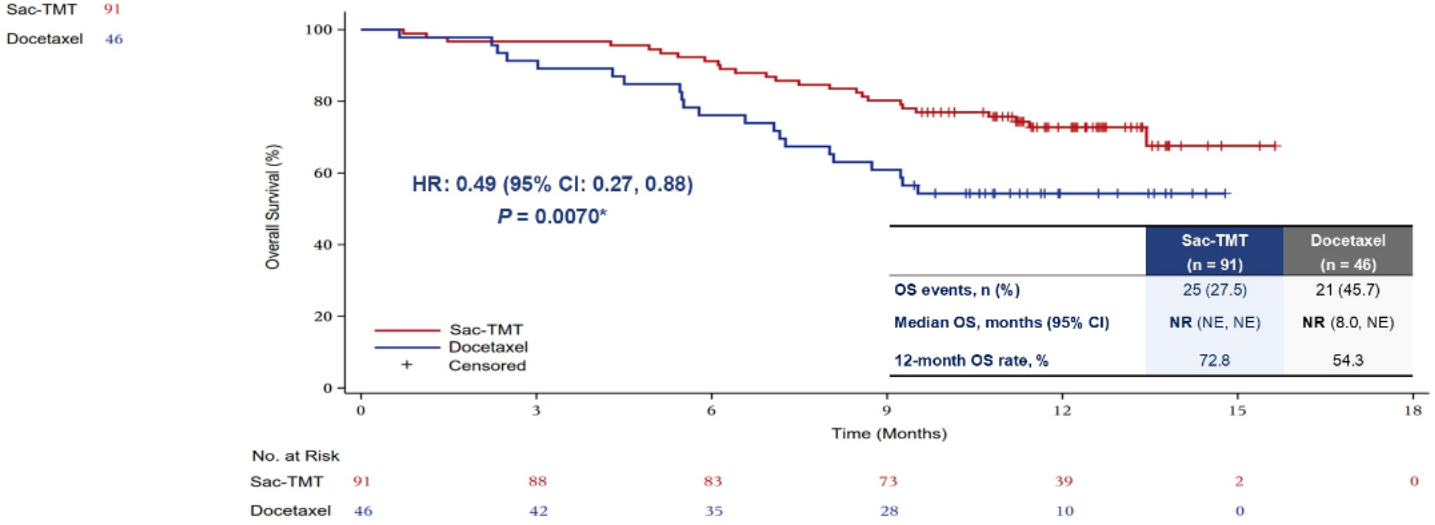
P < 0.0001

Overall Survival

At the interim analysis, Sac-TMT significantly improved OS over docetaxel with 51% lower risk of death.



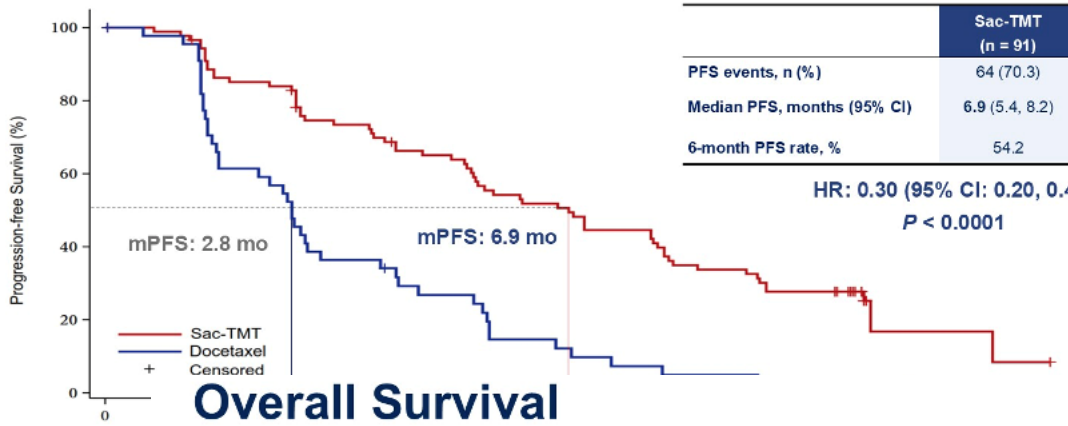
	Sac-TMT (n = 91)	Docetaxel (n = 46)
OS events, n (%)	25 (27.5)	21 (45.7)
Median OS, months (95% CI)	**NR** (NE, NE)	**NR** (8.0, NE)
12-month OS rate, %	72.8	54.3

EGFR 3º Linea

Oral Abstract 8507. OptiTROP- 03. Sac- TMT (antiTROP2) vs Docetaxel

Obejtivo: ORR. Crossover

Sac-TMT significantly improved PFS over docetaxel with 70% lower risk of disease progression or death.



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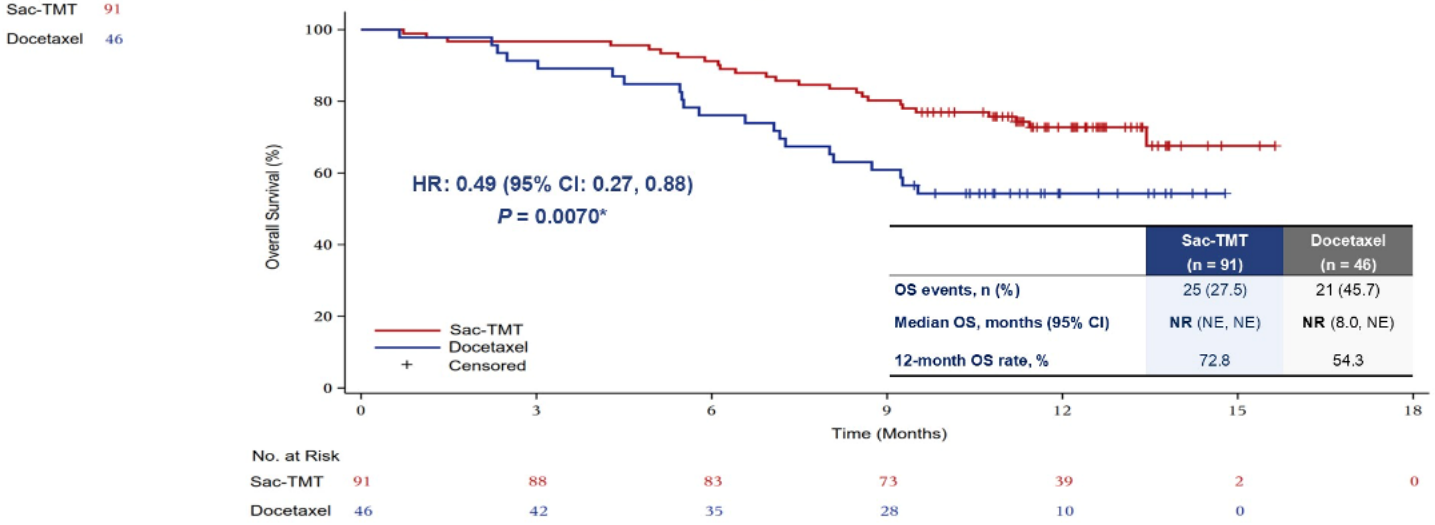
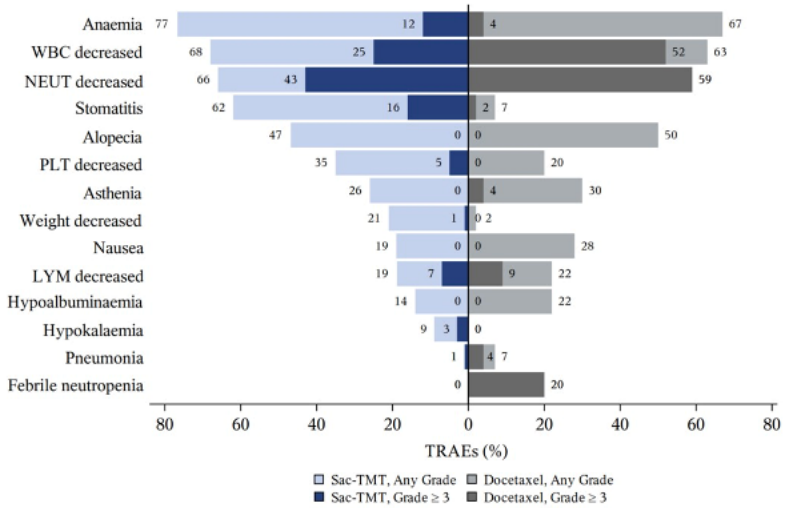


	Sac-TMT (n = 91)	Docetaxel (n = 46)
OS events, n (%)	25 (27.5)	21 (45.7)
Median OS, months (95% CI)	**NR** (NE, NE)	**NR** (8.0, NE)
12-month OS rate, %	72.8	54.3

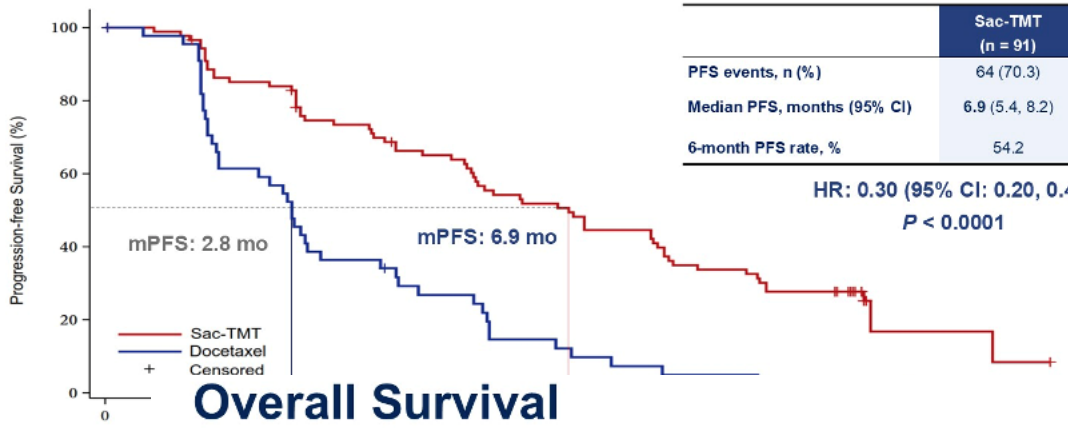


EGFR 3º Linea

Oral Abstract 8507. OptiTROP- 03. Sac- TMT (antiTROP2) vs Docetaxel

Obejtivo: ORR. Crossover

Sac-TMT significantly improved PFS over docetaxel with 70% lower risk of disease progression or death.

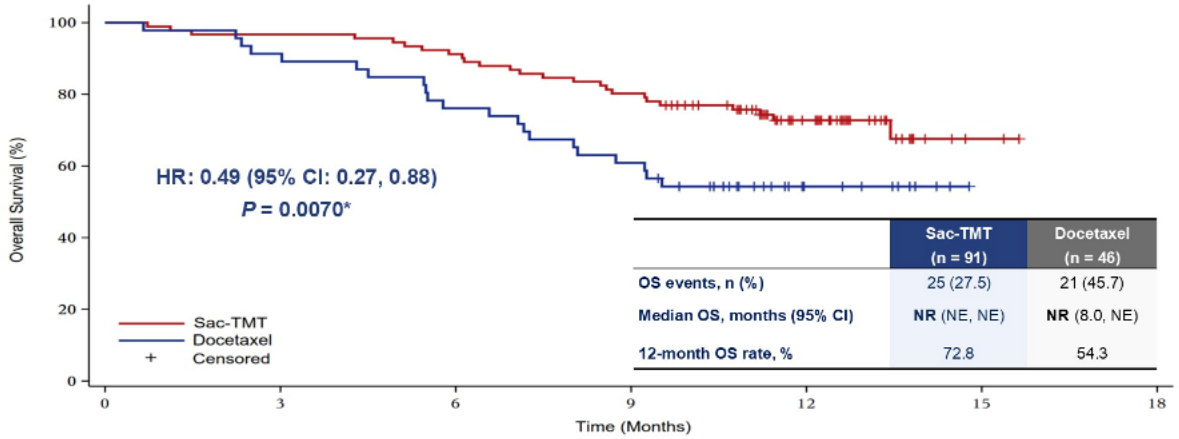


	Sac-TMT (n = 91)	Docetaxel (n = 46)
PFS events, n (%)	64 (70.3)	42 (91.3)
Median PFS, months (95% CI)	**6.9** (5.4, 8.2)	**2.8** (1.6, 4.1)
6-month PFS rate, %	54.2	14.6

HR: 0.30 (95% CI: 0.20, 0.46)
P < 0.0001

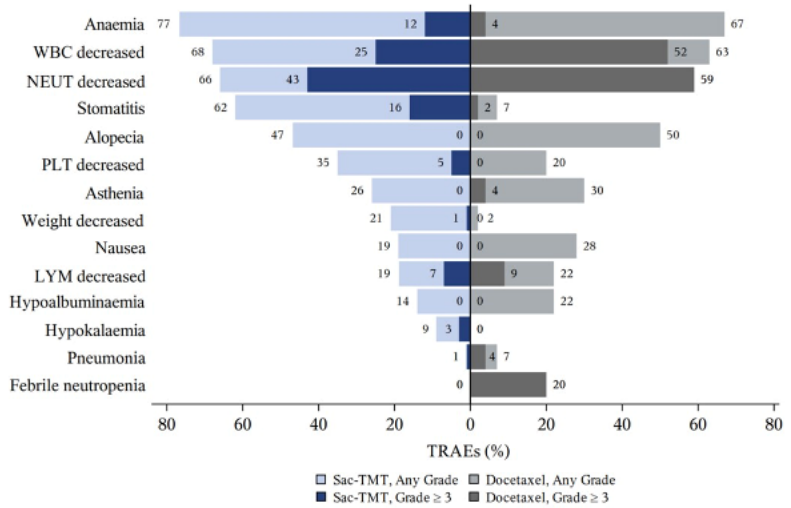
Overall Survival

At the interim analysis, Sac-TMT significantly improved OS over docetaxel with 51% lower risk of death.



	Sac-TMT (n = 91)	Docetaxel (n = 46)
OS events, n (%)	25 (27.5)	21 (45.7)
Median OS, months (95% CI)	**NR** (NE, NE)	**NR** (8.0, NE)
12-month OS rate, %	72.8	54.3

No. at Risk							
Sac-TMT	91	88	83	73	39	2	0
Docetaxel	46	42	35	28	10	0	



Sin casos de NEUMONITIS

EGFR. Brain mets after 1-2G TKI

Oral abstract 2004. Asandeurtenib TY 9591 Phase 1

Significantly Reduces Toxic Metabolites of Osimertini via Deuteration Technology

- Structural similarity to osimertinib, with comparable efficacy and development potential.
- Deuteration technology enhances metabolic stability by blocking key metabolic sites, thus significantly **reduces formation of the toxic metabolite TY-9591-D1 (AZ5104).**
- Potential for improved efficacy and lower toxicity, leading to a broader therapeutic window.

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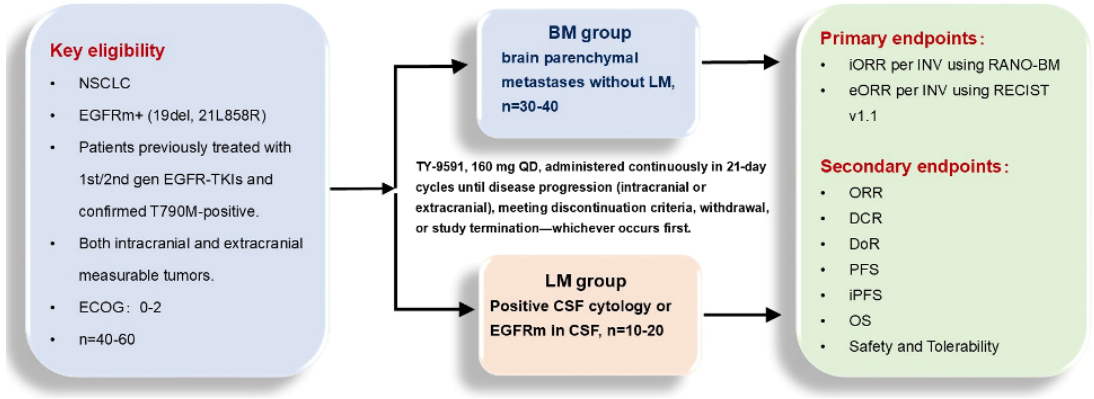

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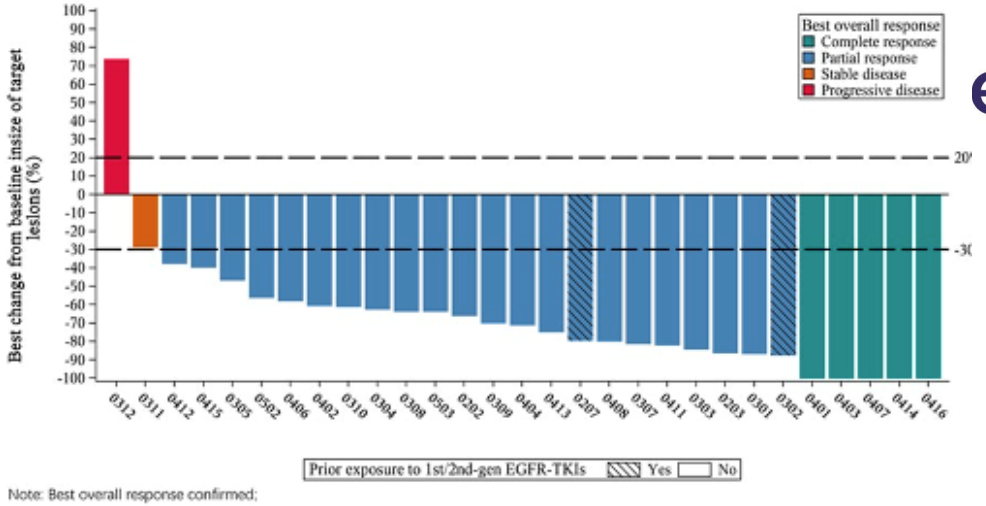
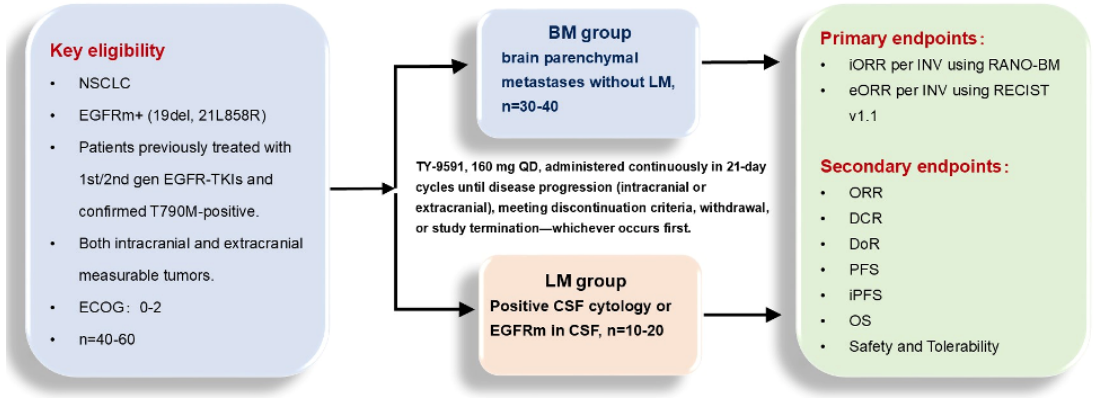


Note: Best overall response confirmed;

Figure 2. Waterfall plot of the best variation of the sum of the longest diameters of intracranial target lesions from baseline



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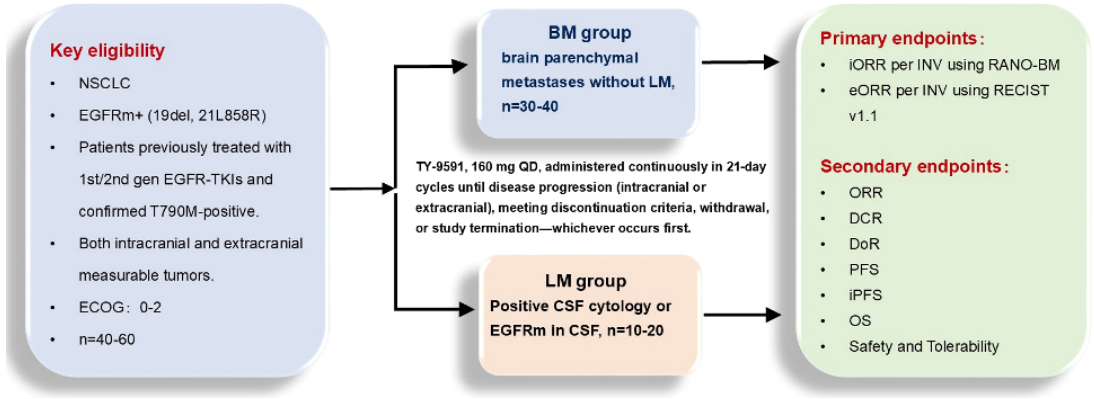

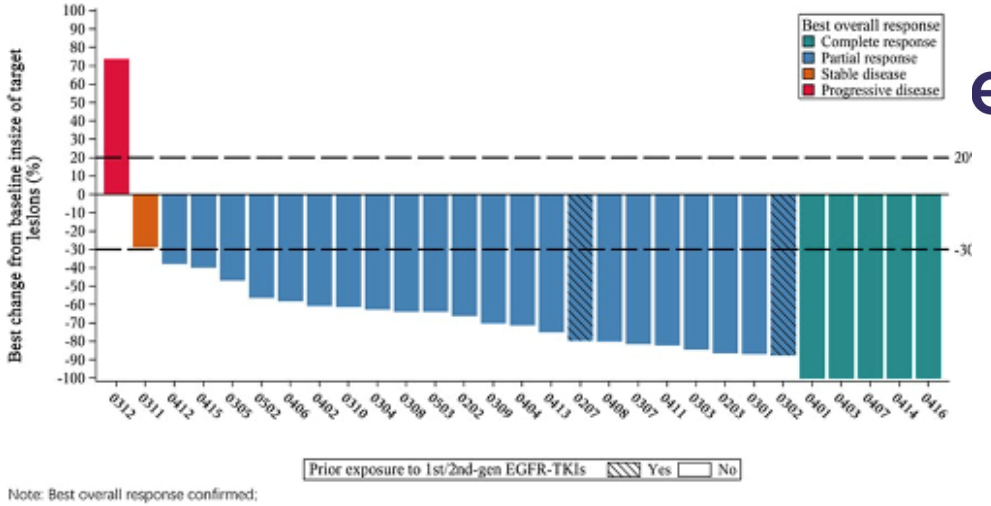

Note: Best overall response confirmed;

Figure 2. Waterfall plot of the best variation of the sum of the longest diameters of intracranial target lesions from baseline

- Asandeutertinib treatment showed improvement in ORR, DCR, iPFS and PFS.
- Median iPFS, DOR, and OS were not reached when the trial was completed.

Table 3. Secondary Efficacy Results

	ORR (%; 95%CI)	DCR (%; 95%CI)	PFS (months; 95%CI)	iPFS (months; 95%CI)	12m-iPFS (%; 95%CI)
All patients (n=29)	82.8 (64.2 - 94.2)	96.6 (82.2 - 99.9)	13.5 (12.5 - NA)	NA (14.7 - NA)	96.6 (77.9 - 99.5)
Treatment naïve (n=27)	81.5 (61.9 - 93.7)	96.3 (81.0 - 99.9)	15.1 (12.5 - NA)	NA	96.3 (76.5-99.5)

EGFR. Brain mets after 1-2G TKI

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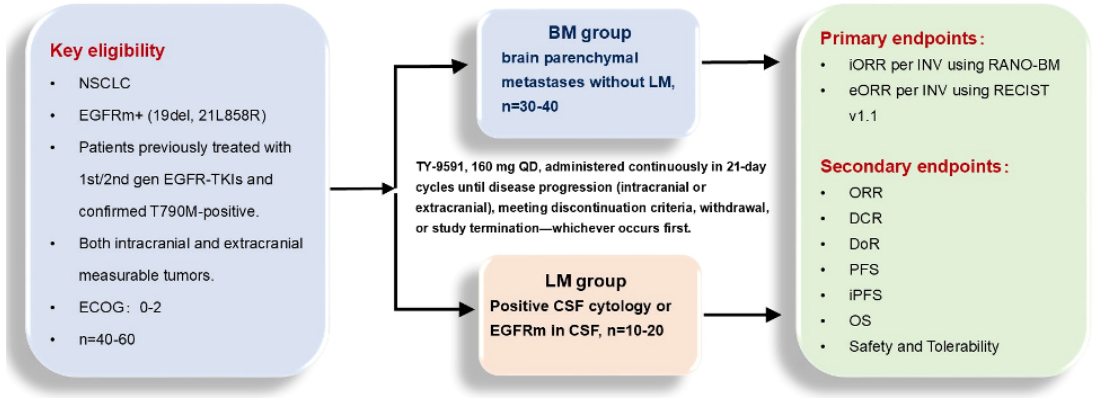

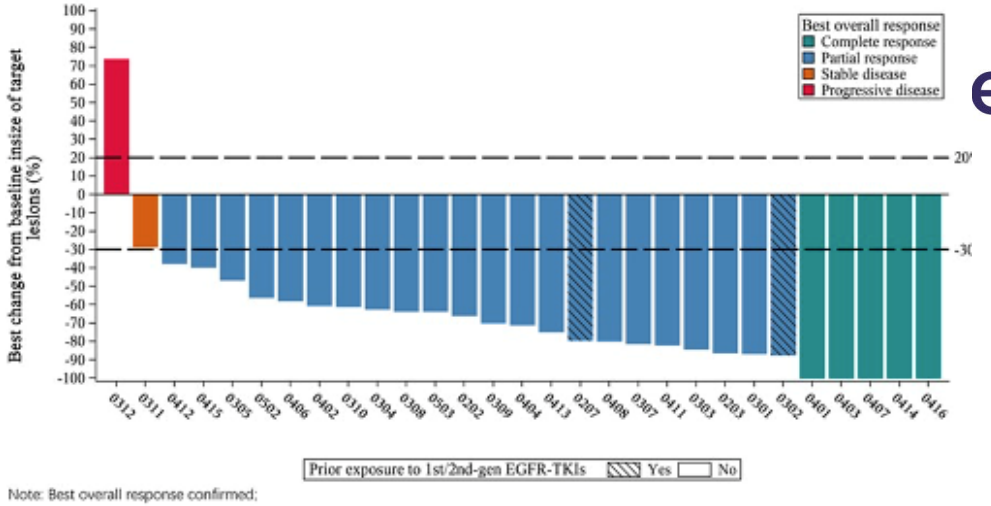

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Treatment naïve (n=27)	81.5 (61.9 - 93.7)	96.3 (81.0 - 99.9)	15.1 (12.5 - NA)	NA	96.3 (76.5-99.5)

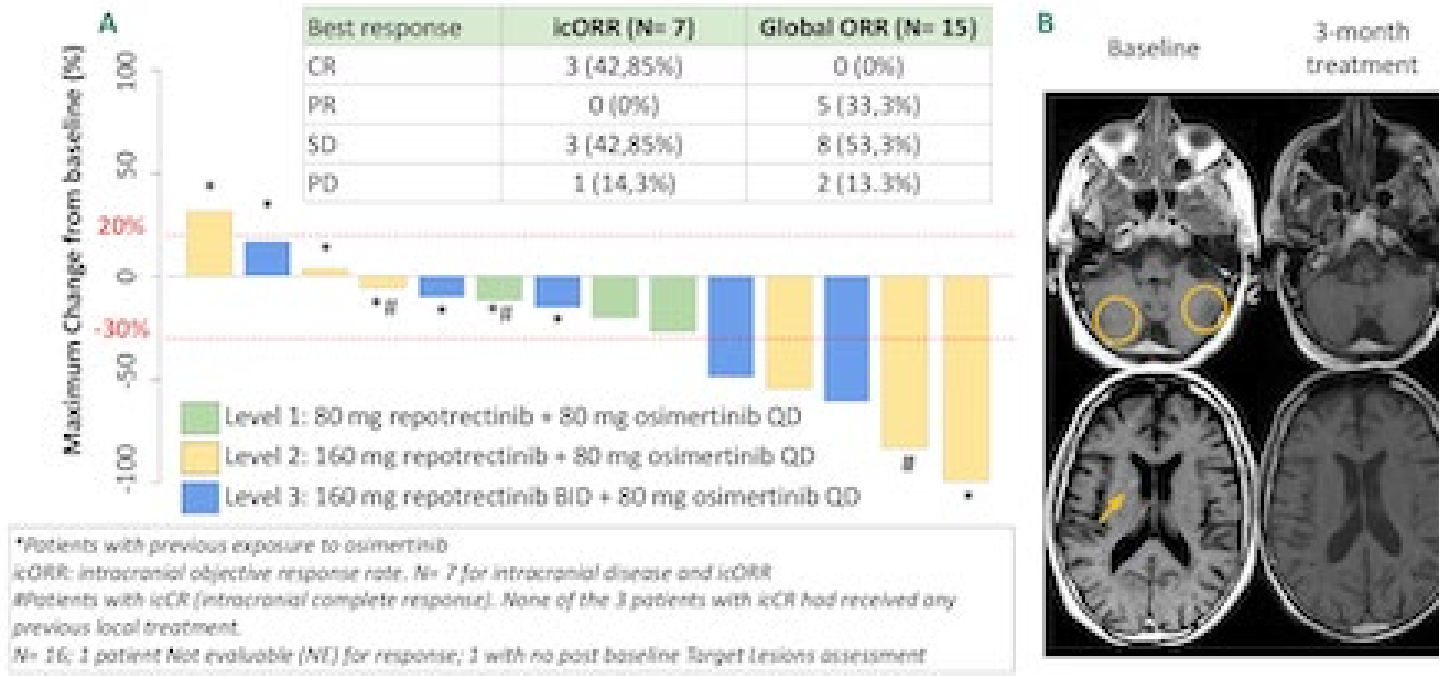
FASE III VS OSIMERTINIB EN BM

EGFR

Poster Abstract 8604. TOTEM Phase 1. Osimertinib + Repotrectinib

Repotrectinib:
Preclinical observation
Osimertinib-induced Src and FAK phosphorylation was abrogated with Repotrectinib.
Hypothesis: Carry on trial osimertinib plus Repotrectinib which inhibit Src/FAK/JAK2, in addition to ALK, ROS1 and NTRKs.

Figure 1 A. Objective response rate (ORR) and target lesions maximum size reduction
B. Example of intracranial response to repotrectinib plus osimertinib in a patient resistant to osimert



Efectos adversos similares a ya reportados.
Pendiente resultados 1B completada

EGFR EXON 20

Oral Abstract. 8503. REZILIENT 1. Zipalertinib in pretreated Chemo +/- Amivantamab

Characteristic	Platinum-based chemotherapy without ex20ins-targeted therapy (n=143)	Prior ex20ins-targeted therapy (n=101)
Median number of prior systemic regimens, No. (range)	1 (0–6)	2 (1–7)
Prior chemotherapy, No. (%)	132 (92)	96 (95)
Prior anti–PD-(L)1, No. (%)	67 (47)	46 (46)
Prior targeted therapy, No. (%)	37 (26)	101 (100)
Amivantamab	0	84 (83)
Mobocertinib	0	40 (40)
Bevacizumab	14 (10)	16 (16)
Osimertinib	13 (9)	7 (7)
BLU-451	0	5 (5)
Cetuximab	4 (3)	0
Poziotinib	0	3 (3)
Sunvozertinib	0	3 (3)

Piotrowska Z. JCO 2025

EGFR EXON 20

Oral Abstract. 8503. REZILIENT 1. Zipalertinib in pretreated Chemo +/- Amivantamab

Outcome	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)[a]
atients with prior r ex20ins-target therapy			
CR	1 (1)	0	1 (2)
PR	61 (35)	50 (40)	11 (22)
Unconfirmed PR[c]	7 (4)	6 (5)	1 (2)
SD	88 (50)	55 (44)	33 (65)
PD	11 (6)	8 (6)	3 (6)
Not evaluable[d]	8 (5)	6 (5)	0
Confirmed ORR, No. (%) [95% CI][e]	62 (35) [28–43]	50 (40) [31–49]	12 (24) [13–38]
DCR, No. (%) [95% CI][f]	157 (89) [84–93]	111 (89) [82–94]	46 (90) [79–97]
CBR, No. (%) [95% CI][g]	113 (64) [57–71]	85 (68) [59–76]	28 (55) [40–69]
Median time to response, days (range)	44 (31–295)	44 (39–232)	44 (39–232)
Median DOR, months (95% CI)	8.8 (8.3–12.7)	8.8 (8.3–12.7)	8.5 (4.2–14.8)

Piotrowska Z. JCO 2025

EGFR EXON 20

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Piotrowska Z. JCO 2025

EGFR EXON 20

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Outcome	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)[a]
BOR, No. (%)[a]			
CR	1 (1)	0	1 (2)
PR	61 (35)	50 (40)	11 (22)
Unconfirmed PR[c]	7 (4)	6 (5)	1 (2)
SD	88 (50)	55 (44)	33 (65)
PD	11 (6)	8 (6)	3 (6)
Not evaluable[d]	8 (5)	6 (5)	0
Confirmed ORR, No. (%) [95% CI][e]	62 (35) [28–43]		
DCR, No. (%) [95% CI][f]	157 (89) [84–93]		
CBR, No. (%) [95% CI][g]	113 (64) [57–71]		
Median time to response, days (range)	44 (31–295)		
Median DOR, months (95% CI)	8.8 (8.3–12.7)		

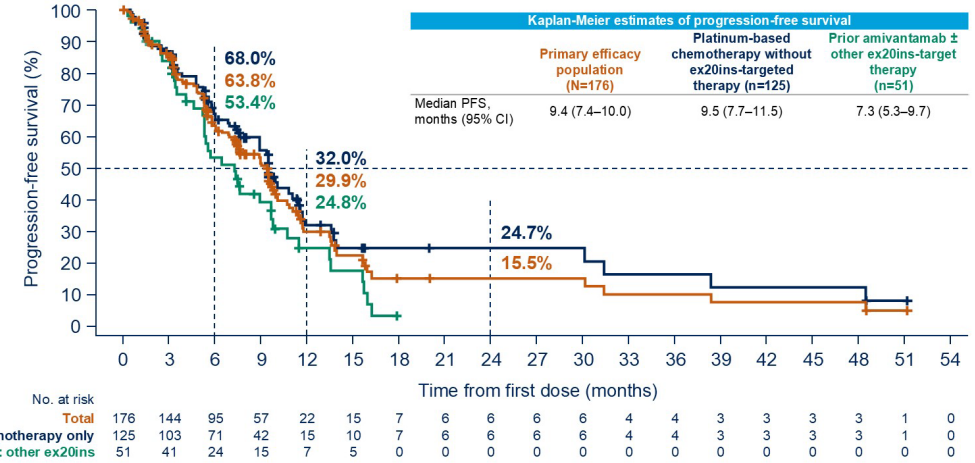
Outcome	Prior amivantamab without other ex20ins-targeted therapy (n=30)	Prior amivantamab and other ex20ins-targeted therapy (n=21)
BOR, No. (%)[a]		
CR	1 (3)	0
PR	8 (27)	3 (14)
Unconfirmed PR[b]	1 (3)	0
SD	19 (63)	14 (67)
PD	0	3 (14)
Confirmed ORR, No. (%) [95% CI][c]	9 (30) [15–49]	3 (14) [3–36]
DCR, No. (%) [95% CI][d]	29 (97) [83–100]	17 (81) [58–95]
CBR, No. (%) [95% CI][e]	18 (60) [41–77]	10 (48) [26–70]
Median time to response, days (range)	43 (39–232)	98 (40–103)
Median DOR, months (95% CI)	14.7 (4.2–NE)	4.2 (3.9–NE)

Piotrowska Z. JCO 2025

EGFR EXON 20

Oral Abstract. 8503. REZILIENT 1. Zipalertinib in pretreated Chemo +/- Amivantamab

Progression-free survival per ICR



Kaplan-Meier estimates of progression-free survival

	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)
Median PFS, months (95% CI)	9.4 (7.4–10.0)	9.5 (7.7–11.5)	7.3 (5.3–9.7)

No. at risk

Total	176	144	95	57	22	15	7	6	6	6	6	4	4	3	3	3	3	1	0
Platinum-based chemotherapy only	125	103	71	42	15	10	7	6	6	6	6	4	4	3	3	3	3	1	0
Prior amivantamab ± other ex20ins	51	41	24	15	7	5	0	0	0	0	0	0	0	0	0	0	0	0	0

Progression-free survival was defined as the time between the day of the first dose of zipalertinib and the first documentation of progressive disease or death, whichever occurred earlier.
CI, confidence interval; ex20ins, exon 20 insertions; ICR, independent central review; PFS, progression-free survival.

Piotrowska Z. JCO 2025
Corassa M. ASCO 2025

EGFR EXON 20

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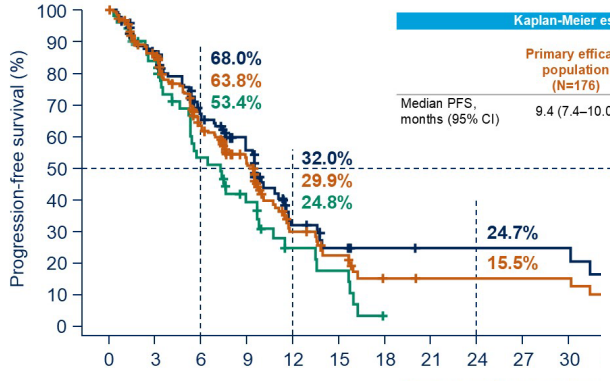

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No. at risk											
Total	176	144	95	57	22	15	7	6	6	6	6
Platinum-based chemotherapy only	125	103	71	42	15	10	7	6	6	6	6
Prior amivantamab ± other ex20ins	51	41	24	15	7	5	0	0	0	0	0

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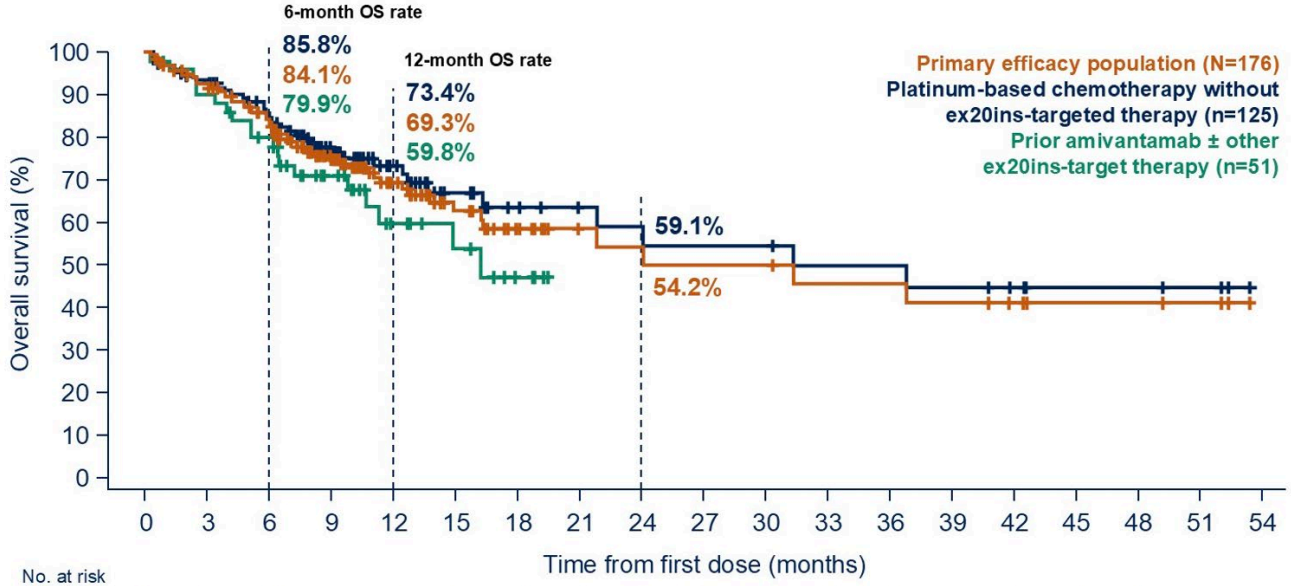
ASCO MEETING #ASCO25

PRESENTED BY: Helena Alexandra Yu, MD

Overall survival



No. at risk																			
Total	176	158	137	88	51	32	21	14	13	12	12	10	10	9	7	5	5	3	0
Platinum-based chemotherapy only	125	113	99	64	38	23	17	14	13	12	12	10	10	9	7	5	5	3	0
Prior amivantamab ± other ex20ins	51	15	38	24	13	9	4	0	0	0	0	0	0	0	0	0	0	0	0

Piotrowska Z. JCO 2025
Corassa M. ASCO 2025

EGFR EXON 20

Oral Abstract. 8503. REZILIENT 1. Zipalertinib in pretreated Chemo +/- Amivantamab

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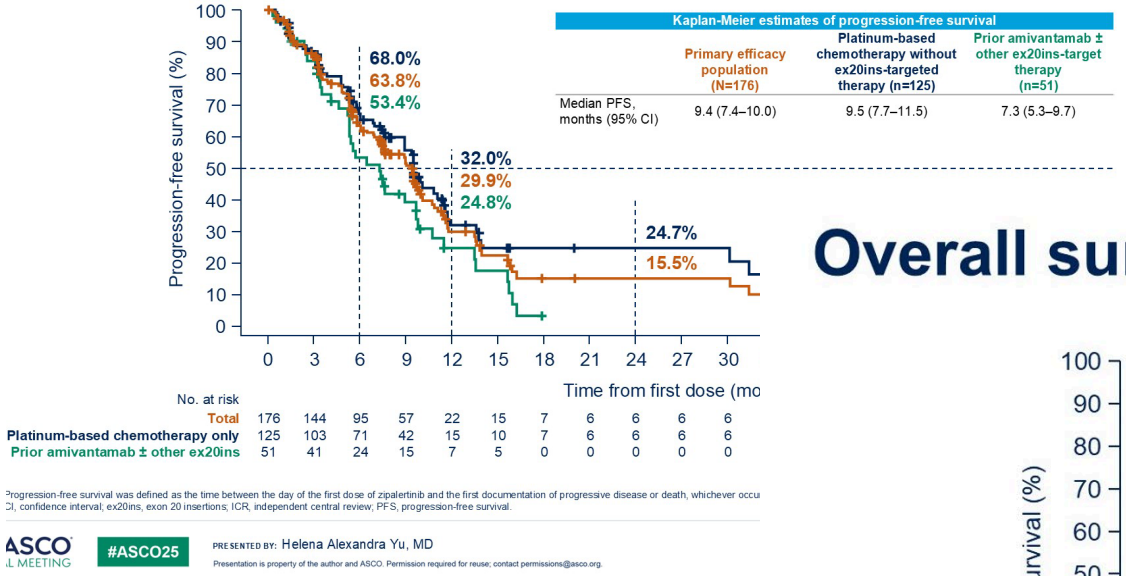

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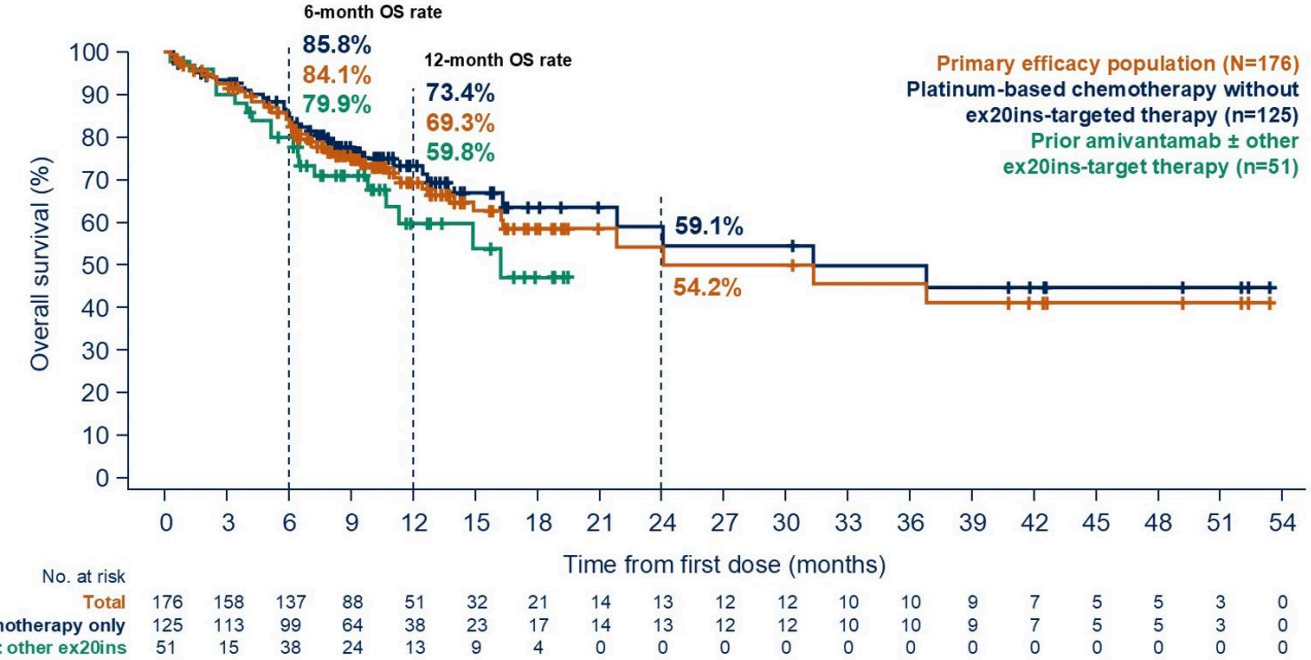
ASCO MEETING #ASCO25

PRESENTED BY: Helena Alexandra Yu, MD

Point #1: Zipalertinib and its partners have similar activity. Sequencing TKIs does not seem to be the best road to follow.

Overall survival



Piotrowska Z. JCO 2025
Corassa M. ASCO 2025

ALK

Abstract 8625. Rare ALK fusions.

29 centers Europeos

Characteristics	EML4::ALK	Rare ALK
Total number of patients	277	51
Age, y, median (25th; 75th percentile)	59 (49; 69)*	66 (53; 72)*
Sex (N = 277, 51), n (%)		
Female	143 (52)	21 (41)
Male	134 (48)	30 (59)
Smoking (N = 266, 49), n (%)		
Active Smoker	32 (12)	11 (22)
Former Smoker	63 (23)	19 (37)
Never Smoker	161 (58)*	19 (37)*
Pack years in smokers, median	6,7*	14,7*
Histology (N=277, 51), n (%)		
Adenocarcinoma	261 (94)	45 (88)
Squamous	4 (1)	5 (10)
Adenosquamous	4 (1)	1 (2)
Undifferentiated / NOS	5 (2)	0 (0)

Mas fumadores

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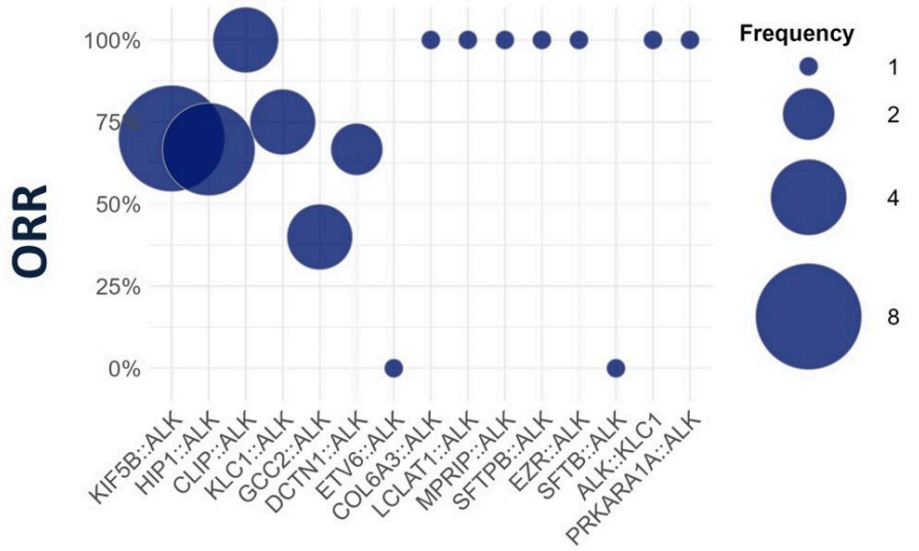


Mas fumadores

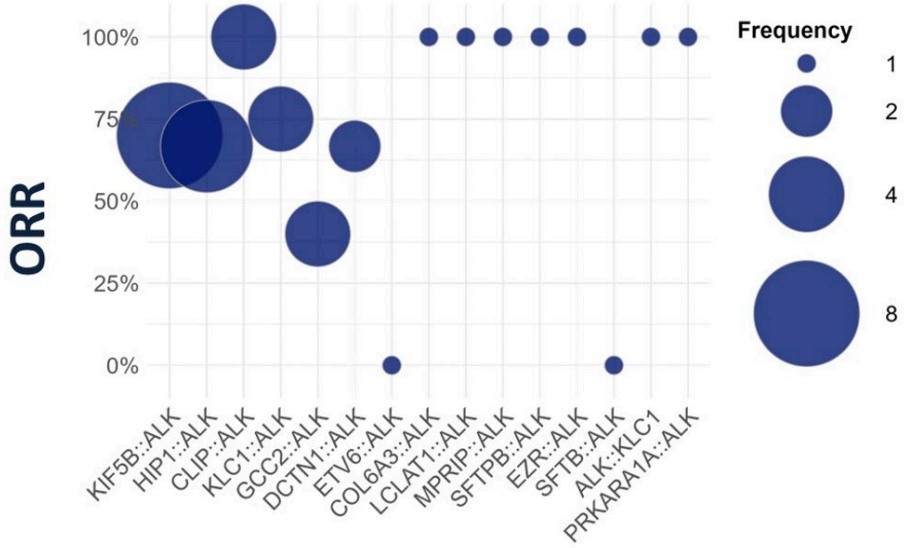
ALK

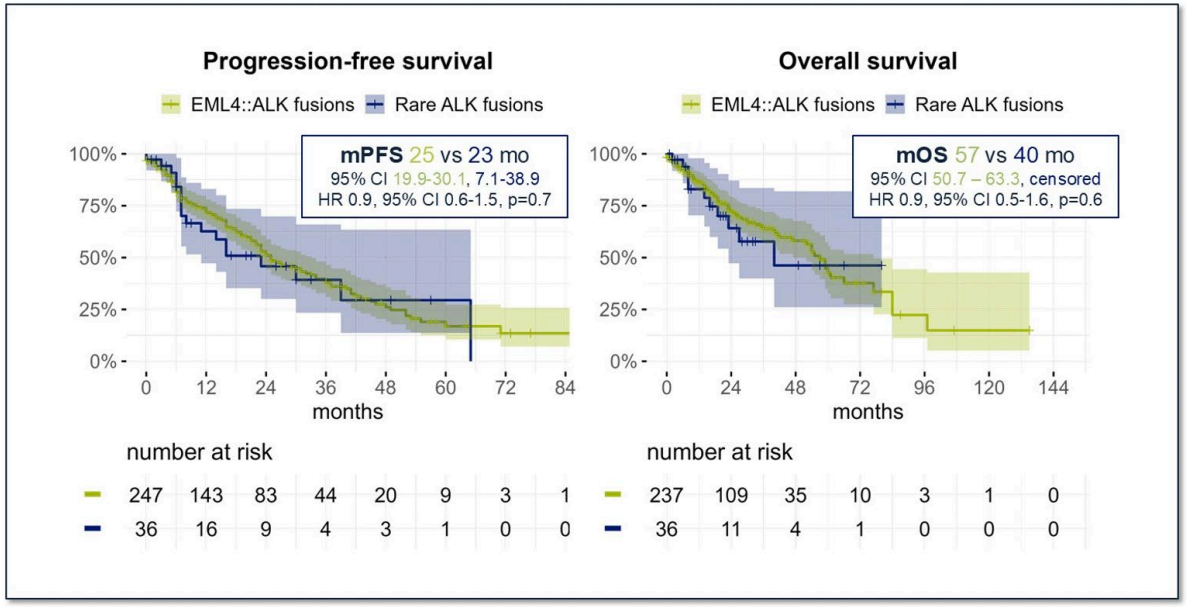
Abstract 8625. Rare ALK fusions.

29 centers Europeos

Characteristics	EML4::ALK	Rare ALK
Total number of patients	277	51
Age, y, median (25th; 75th percentile)	59 (49; 69)*	66 (53; 72)*
Sex (N = 277, 51), n (%)		
Female	143 (52)	21 (41)
Male	134 (48)	30 (59)
Smoking (N = 266, 49), n (%)		
Active Smoker	32 (12)	11 (22)
Former Smoker	63 (23)	19 (37)
Never Smoker	161 (58)*	19 (37)*
Pack years in smokers, median	6,7*	14,7*
Histology (N=277, 51), n (%)		
Adenocarcinoma	261 (94)	45 (88)
Squamous	4 (1)	5 (10)
Adenosquamous	4 (1)	1 (2)
Undifferentiated / NOS	5 (2)	0 (0)

Mas fumadores

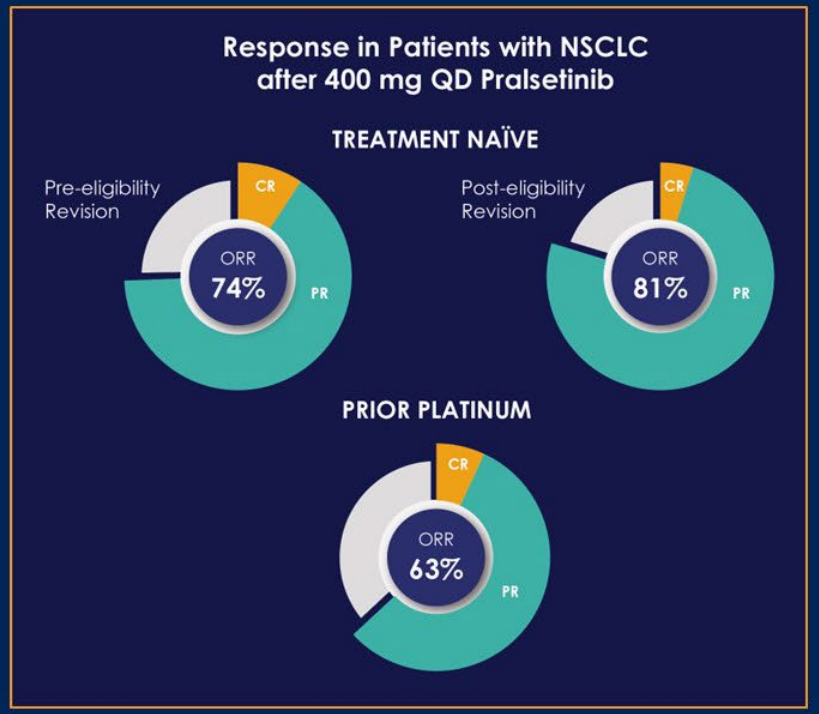


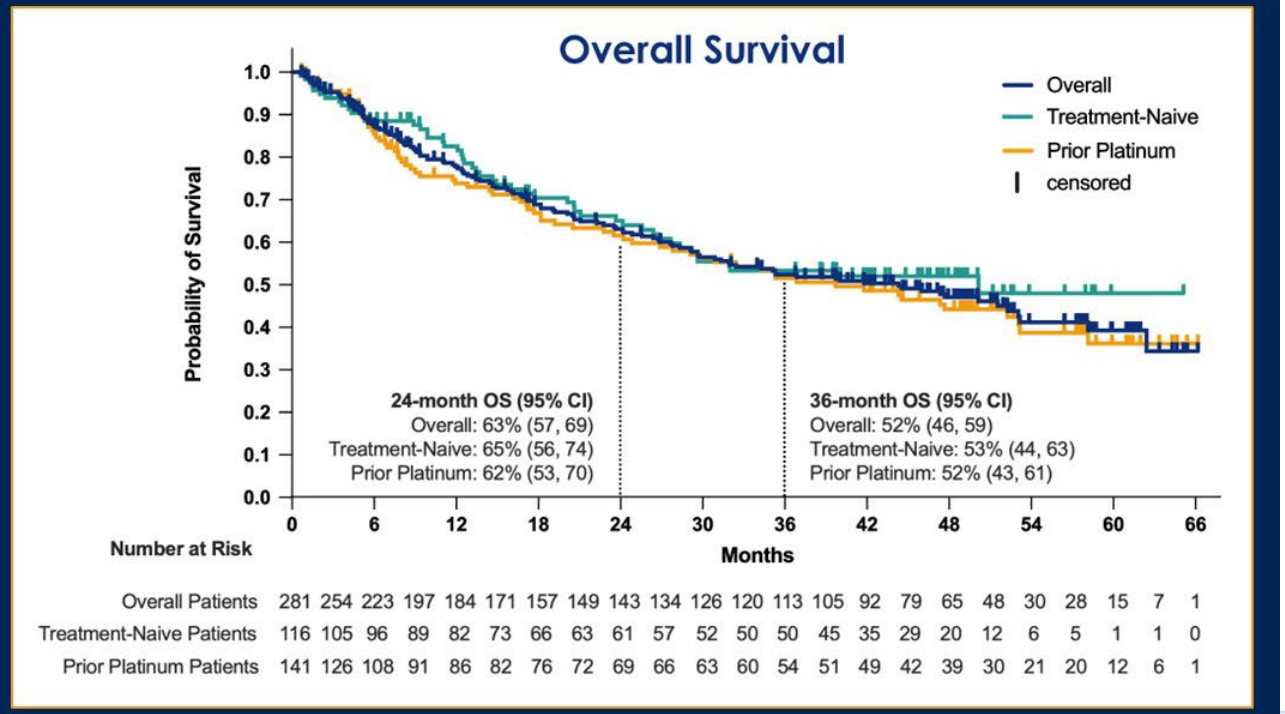


RET

Abstract 3116. AAROW ½ Final data Pralsetinib NSCL

- 281 patients with *RET* fusion-positive NSCLC received pralsetinib 400 mg QD, with a median duration of treatment of 15 months





Subbiah JCO 2020

RET

Abstract RET- MAP registry. Rechallenge First generation TKI

First use of RETi, n=38

ORR 78%
PFS 12.9 months
(95%CI 9.2-30.3)

RETi monotherapy after toxicity, n=11

- All patients received a different RETi
- 3 developed toxicity at rechallenge

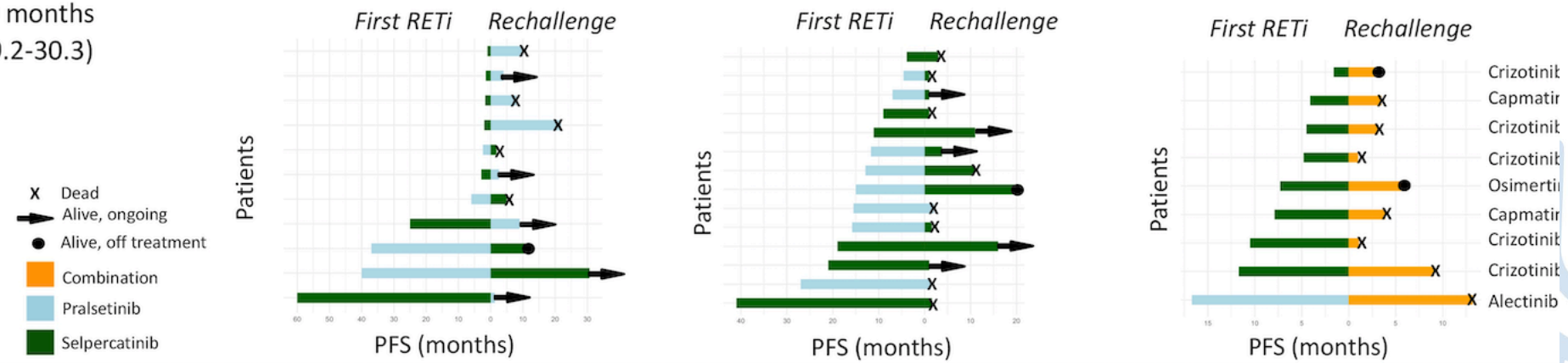
ORR 50%
mPFS: 9.89 (95%CI 5.25-NA)

RETi monotherapy after PD, n=14

ORR 18%
mPFS 2.14 (95%CI 1.61-NA)

RETi plus targeted agents for bypass resistance, n=9

ORR 38%
mPFS 3.94 (95%CI 3.19-NA)



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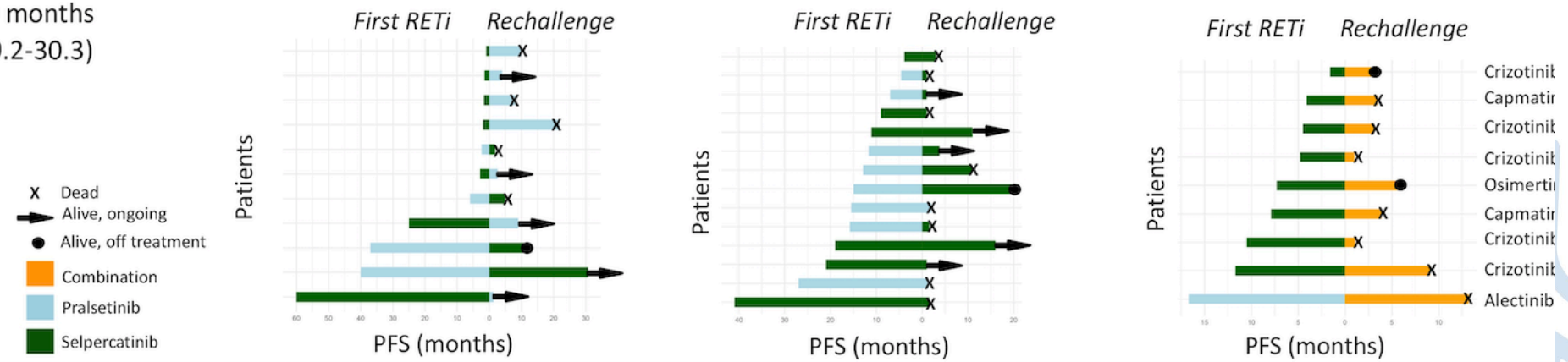


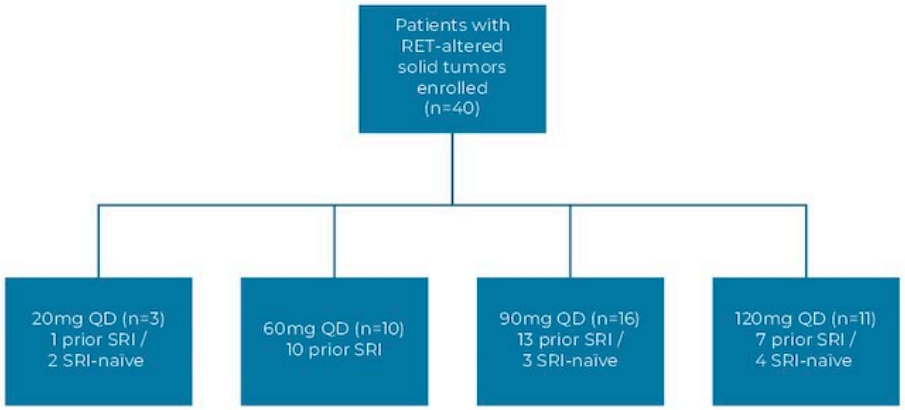
Rechallenge monotherapy after progression: Limited efficacy

Subbiah JCO 2020

RET

Abstract 8598. Phase I EP0031. Naive o pretreated

Figure 1. Study design



Other evaluations

- Tumor biopsy to determine RET gene fusions and mutations and correlation with efficacy

Marinello A. Abstract8646
Alonso Casal. Abastract 8598

RET

Abstract 8598. Phase I EP0031. Naive o pretreated

Figure 1. Study design

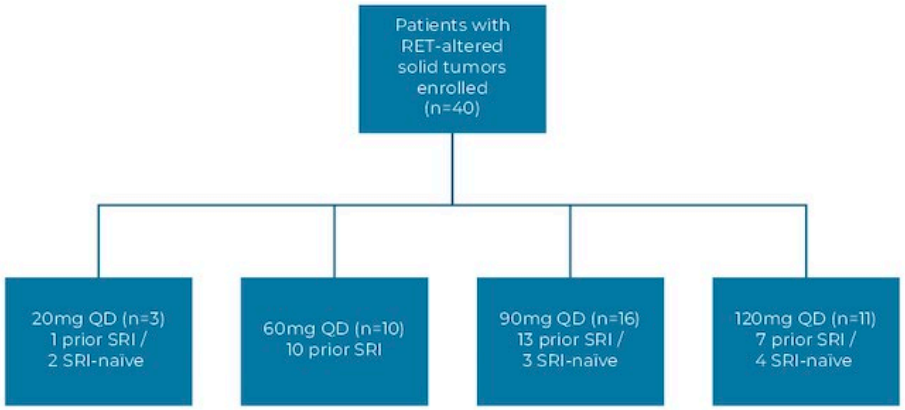


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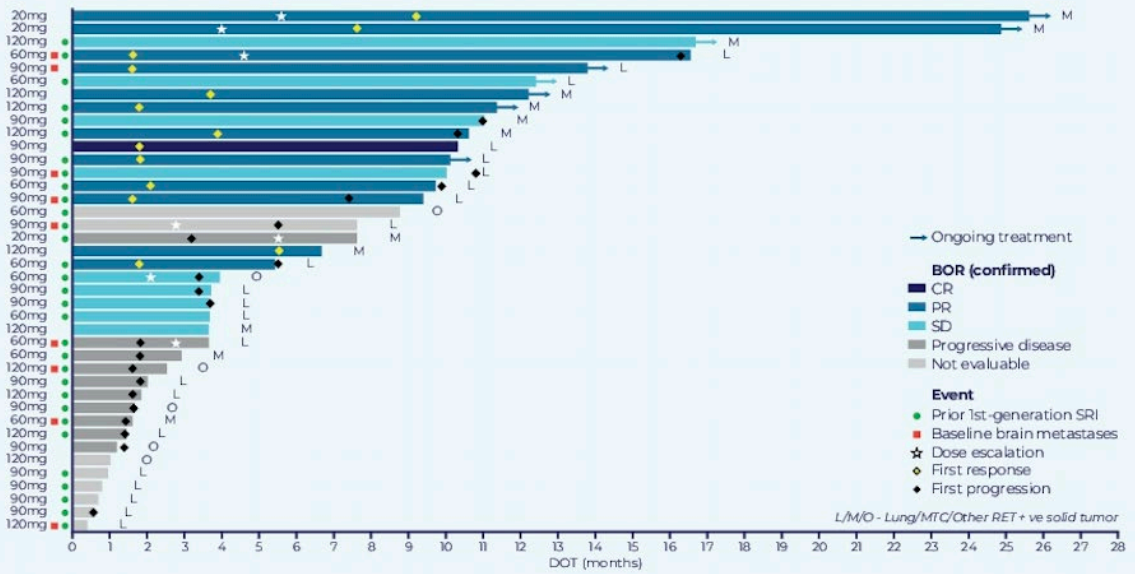
Figure 2. DOT in 40 treated patients



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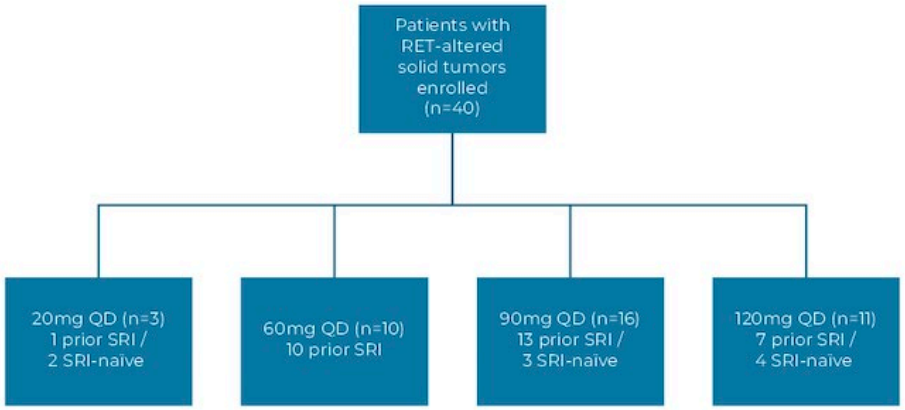

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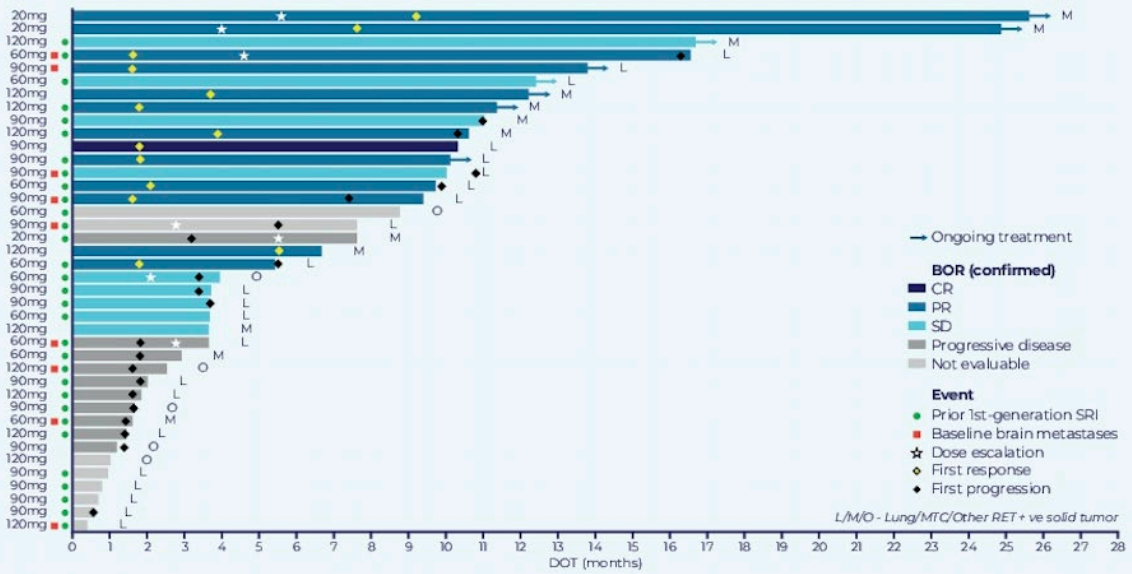


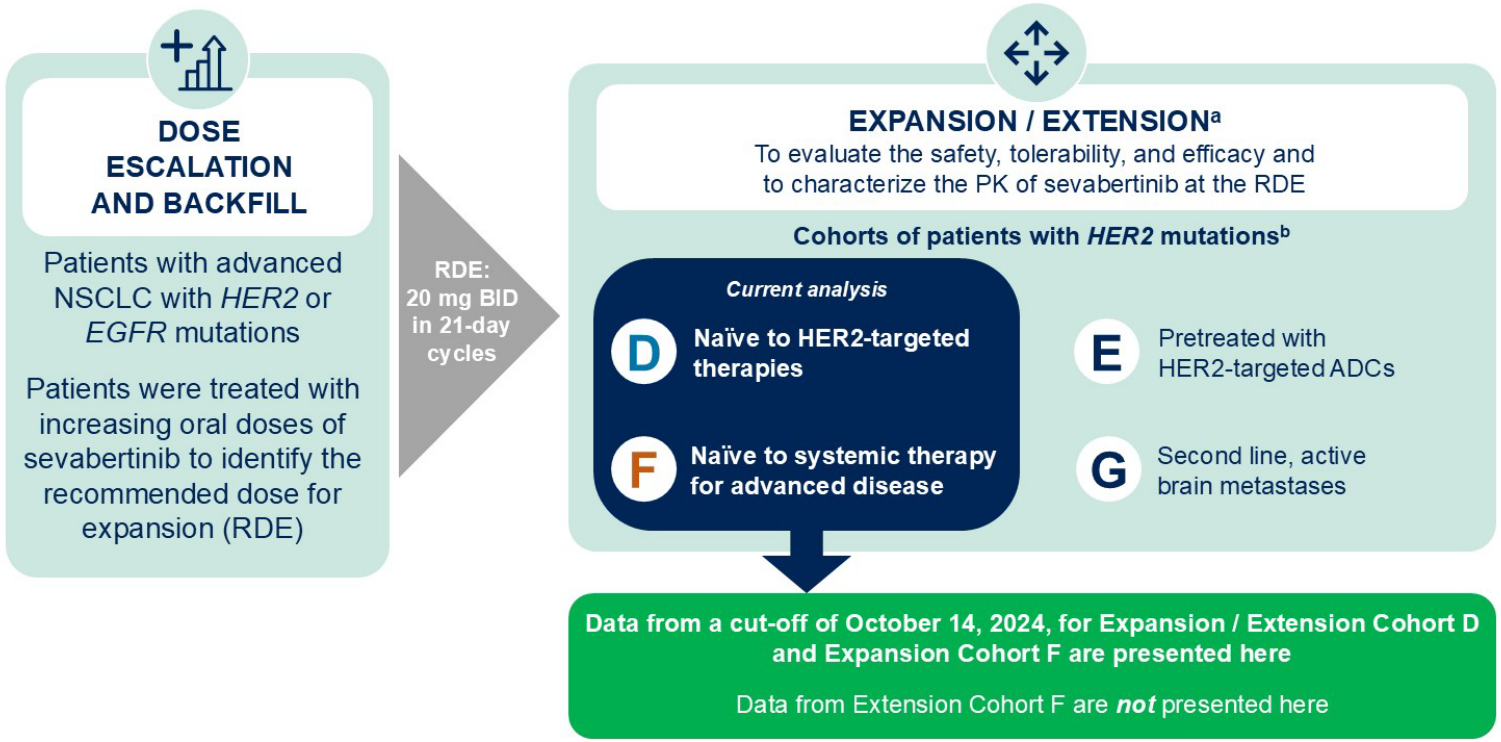
- Shows evidence of deep and durable responses in NSCLC regardless of exposure to prior SRI including selpercatinib and pralsetinib
- Efficacy extends to patients with brain metastases, with complete resolution in several patients
- Showed clearance of on-target RET resistance mutations, namely G810R solvent front (patient with papillary thyroid cancer (PTC), prior selpercatinib) and L730V, L730I RET roof mutations (patient with NSCLC, prior pralsetinib)

Marinello A. Abstract8646
Alonso Casal. Abastract 8598

HER2

Oral Abstract 8504. SOHO-01: Safety and efficacy of BAY 2927088 (Sevabertinib)

SOHO-01 study design (NCT05099172)



PRIMARY ENDPOINTS

- Safety and tolerability
- PK

SECONDARY ENDPOINTS

- ORR (per investigator assessment and BICR) by RECIST v1.1
- DoR, DCR, and PFS (per investigator assessment and BICR)

[a]Patients from dose escalation / backfill treated with 20 mg BID and who met the same eligibility criteria were combined for statistical analysis; [b]Cohorts of patients with *EGFR* mutations are not shown

ADC, antibody-drug conjugate; BICR, blinded independent central review; DCR, disease control rate; DoR, duration of response; EGFR, epidermal growth factor receptor; ORR, objective response rate; PFS, progression-free survival

PRESENTED BY: Dr Herbert H. Loong

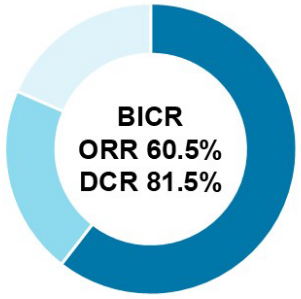
HER2

Oral Abstract 8504. SOHO-01: Safety and efficacy of BAY 2927088 (Sevabertinib)

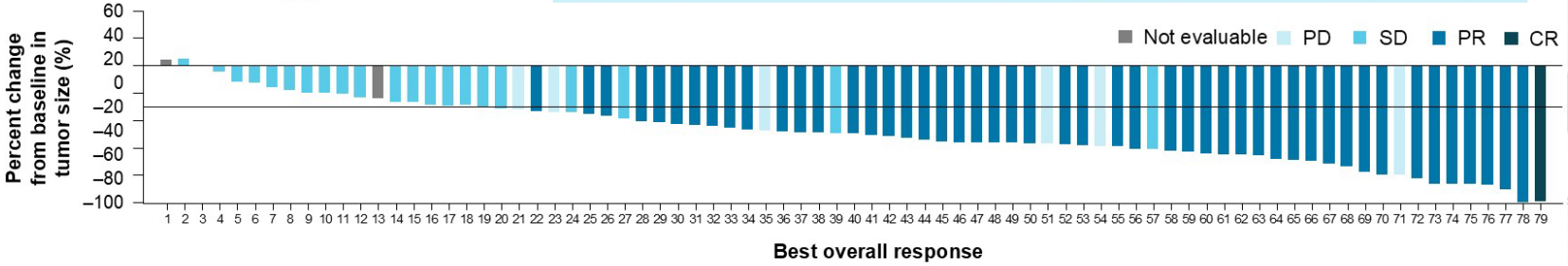
Sevabertinib in pretreated *HER2*-mutant NSCLC (Cohort D): Tumor response by blinded independent central review (BICR)

Cohort D (*n*=81), naïve to HER2-targeted therapy

Median follow-up: 7.3 months[a]



n (%)	INV	BICR
CR	1 (1.2)	1 (1.2)
PR	47 (58.0)	48 (59.3)
SD	22 (27.2)	22 (27.2)
PD	10 (12.3)	7 (8.6)
Not evaluable[b]	1 (1.2)	3 (3.7)
ORR[c] [95% CI]	**48 (59.3)** [47.8, 70.1]	**49 (60.5)** [49.0, 71.2]
DCR[d] [95% CI]	**68 (84.0)** [74.1, 91.2]	**66 (81.5)** [71.3, 89.2]



HER2

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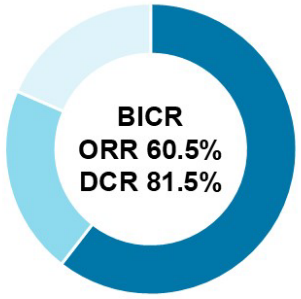

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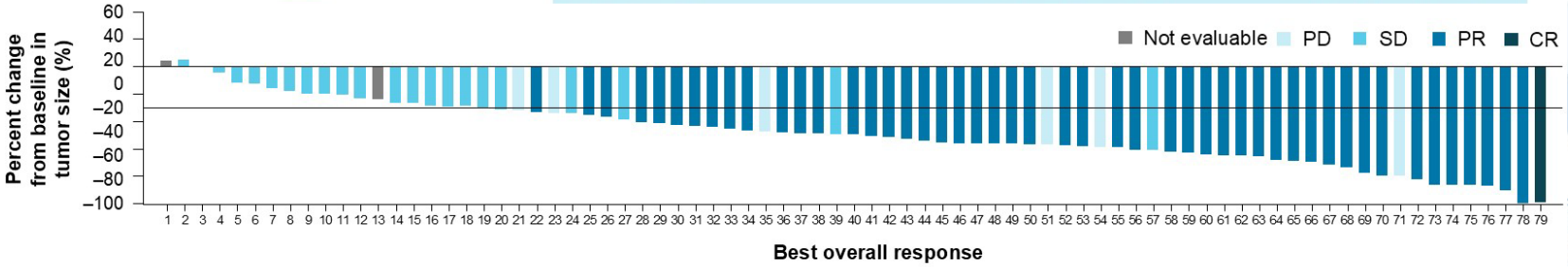

- **Median follow-up was 7.3 months[a]**
- **41 of 81 patients (50.6%) had ongoing treatment**
- **16 patients (19.8%) had a treatment duration of >12 months**
- **Median duration of treatment was 6.2 months (range 0.2-24.4)**

HER2

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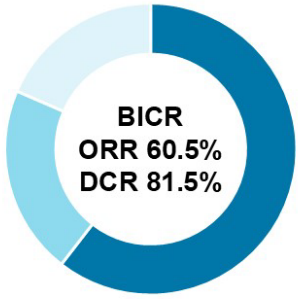

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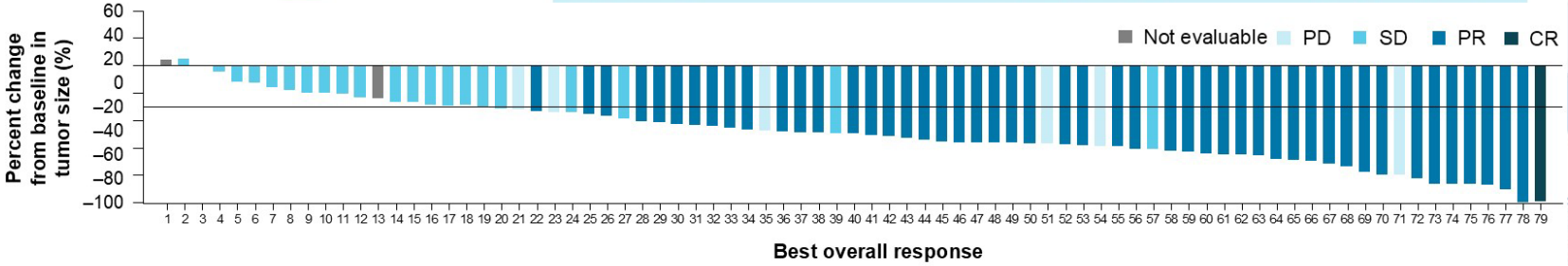

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In Expansion Cohort D (*n*=44)[a]:

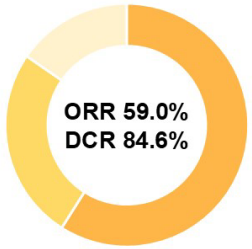
- **Median DoR (95% CI) was 9.2 months (5.2, not estimable); range 2.6-21.5[b] months**
- **12-month DoR rate was 49.3%**
- **48.0% of patients were censored**

HER2

Oral Abstract 8504. SOHO-01: Safety and efficacy of BAY 2927088 (Sevabertinib)

Cohort F: Naïve systemic treatment

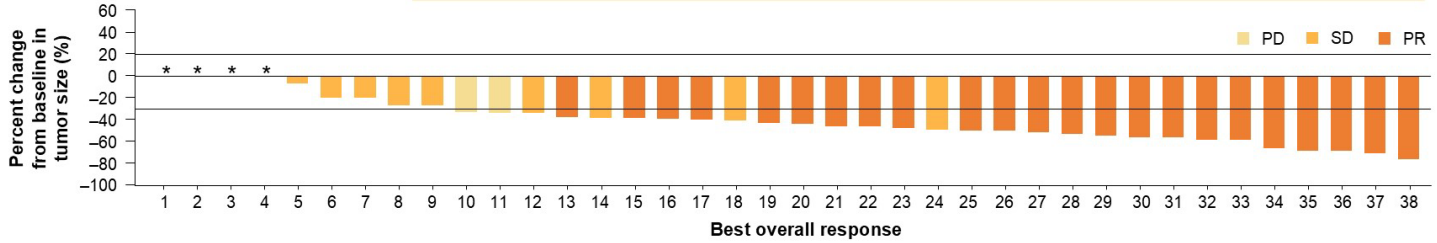
Sevabertinib in first-line *HER2*-mutant NSCLC (Expansion Cohort F): Preliminary tumor response



Cohort F (*n*=39): naïve to systemic therapy for advanced disease

Median follow-up: 5.6 months[a]

n (%)	INV
CR	0
PR	23 (59.0)
SD	12 (30.8)
PD	3 (7.7)
NA[b]	1 (2.6)
ORR[c] [95% CI]	**23 (59.0)** [42.1, 74.4]
DCR[d] [95% CI]	**33 (84.6)** [69.5, 94.1]



Date for patients without a target lesion measurement are not shown in the waterfall plot. Tumor response was assessed by RECIST v1.1.
*Patients exhibited a 0% tumor reduction
[a]Data for Extension Cohort F are immature as of the October 14, 2024, cut-off; [b]Not available: post-baseline tumor assessment, but discontinued due to a drug-related toxicity, death, or progression by clinical judgment before disease was re-evaluated and was therefore considered evaluable (considered as non-responder); [c]Patients with confirmed CR or PR; [d]Patients with confirmed CR or confirmed PR or SD for ≥12 weeks

CI, confidence interval; CR, complete response; DCR, disease control rate; INV, investigator assessed; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

mFollow up: 5.6 m. (2.1% ongoing

HER2

Oral Abstract 8504. SOHO-01: Safety and efficacy of BAY 2927088 (Sevabertinib)

Cohort F: Naïve systemic treatment

Sevabertinib in first-line *HER2*-mutant NSCLC (Ex
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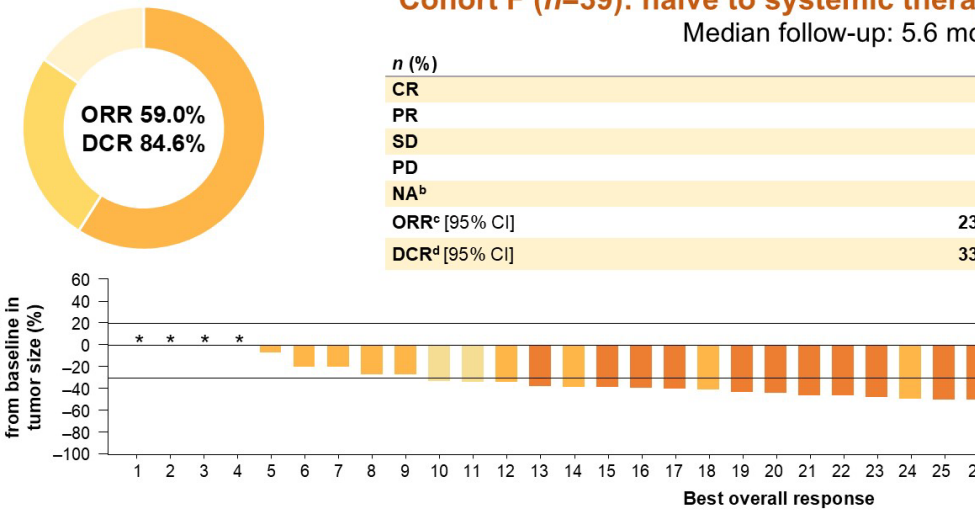

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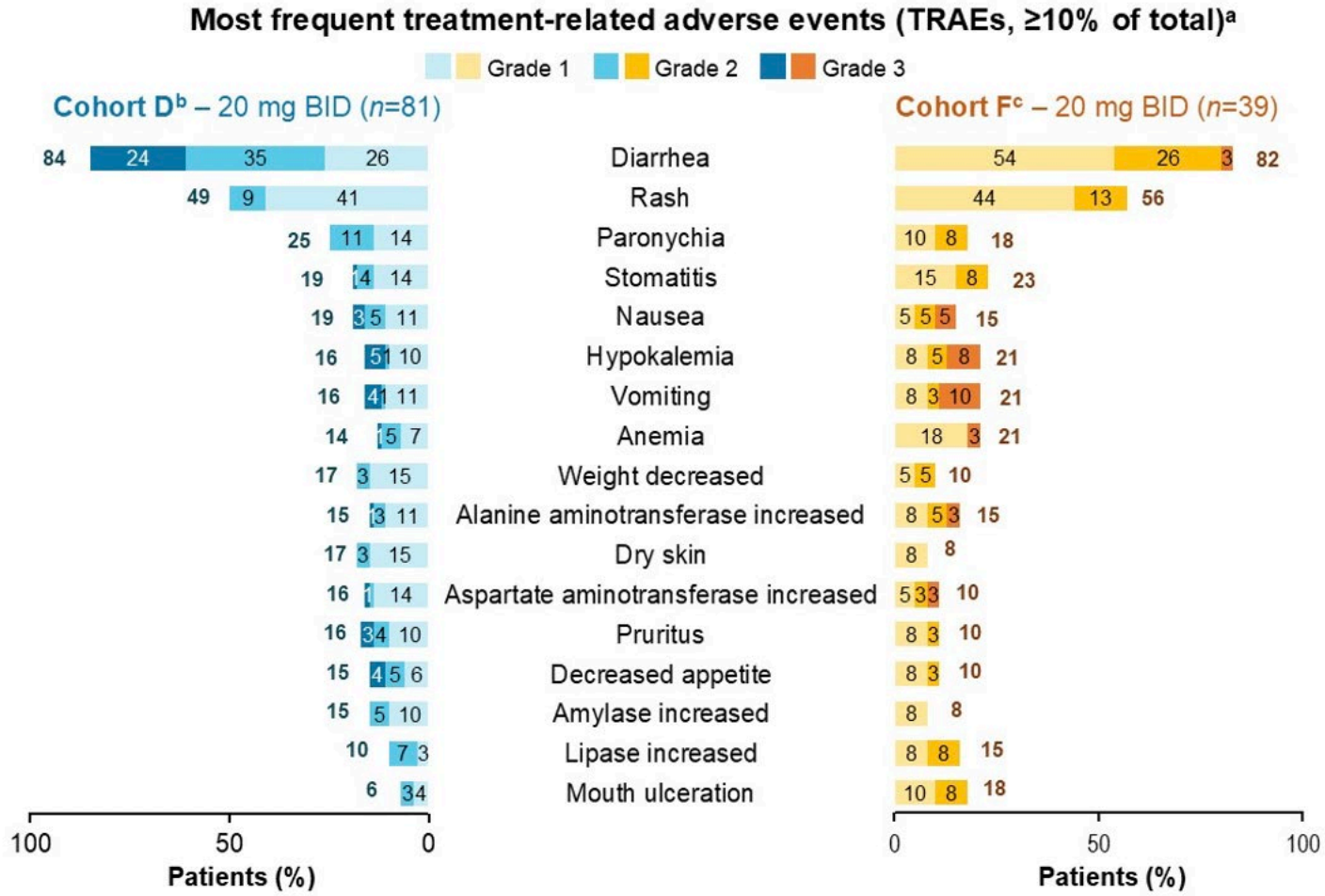

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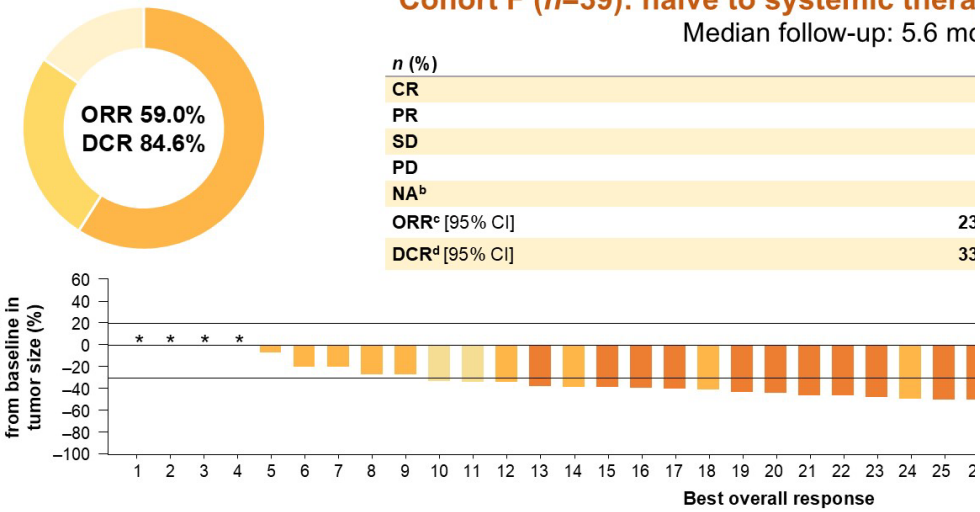

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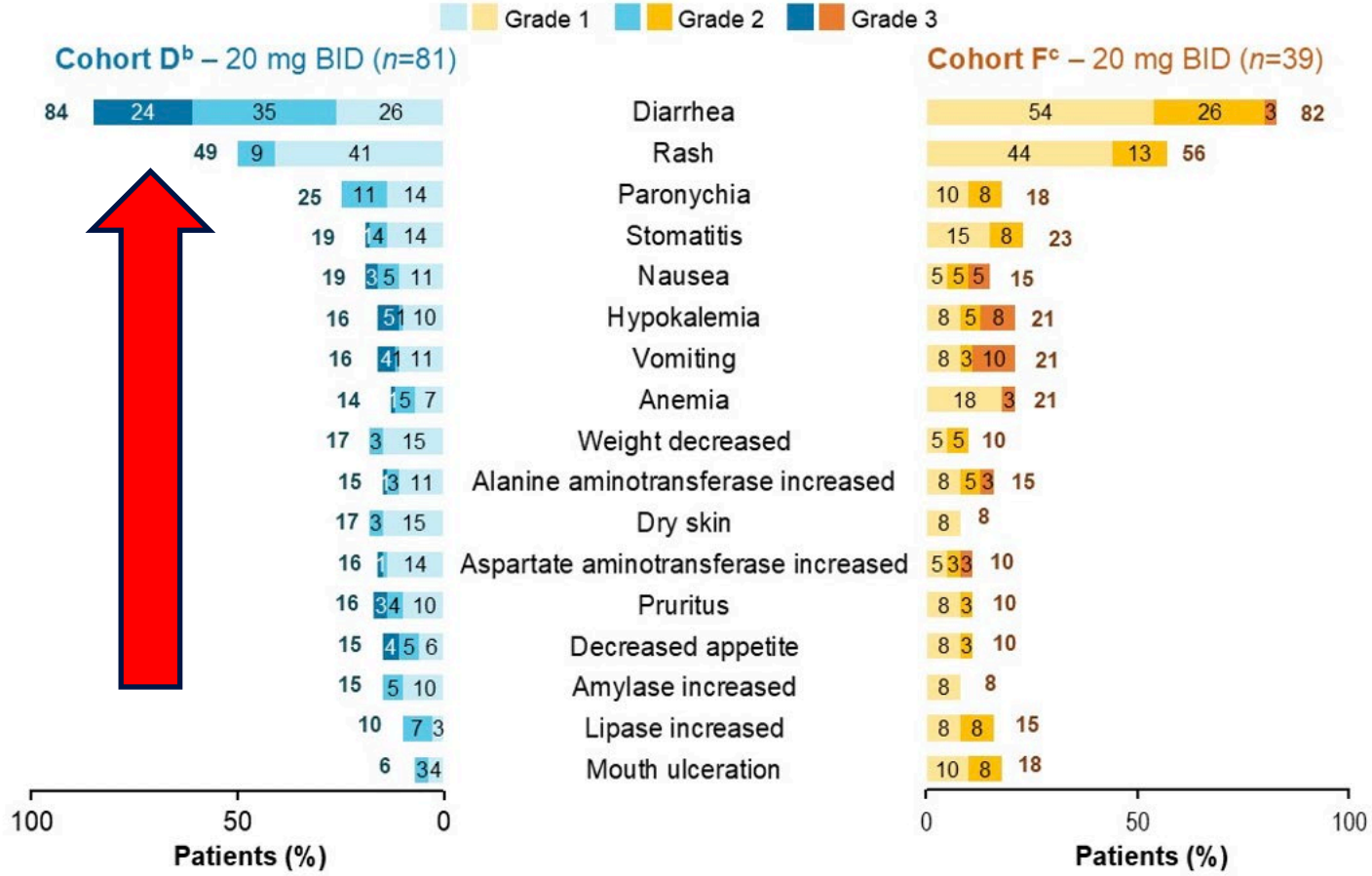
2025 ASCO ANNUAL MEETING #ASCO25 PRESENTED BY: Dr Herbert H. Loong

Most frequent treatment-related adverse events (TRAEs, ≥10% of total)[a]



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HER2

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Alteration	Drug	Population	ORR	mDoR (months)	mPFS	mOS	FDA-Approved
HER2 mutations	T-Dxd	Pretreated	55%	9.3	8.2	17.3	Yes
	T-DM1	Pretreated/Naïve	44%	4.0	5.0	Not Available	No
	THP	Pretreated	29%	11.0	6.8	17.6	No
	Poziotinib	Pretreated/Naïve	27%	5.0	5.5	15.0	No
	Pyrotinib	Pretreated	30%	6.9	6.9	14.4	No
	Afatinib	Pretreated	13%	6.0	3.0	23.0	No

Corassa M. ASCO 2025
Heymatch GV. NEJM 2025

HER2

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Beamion LUNG-1
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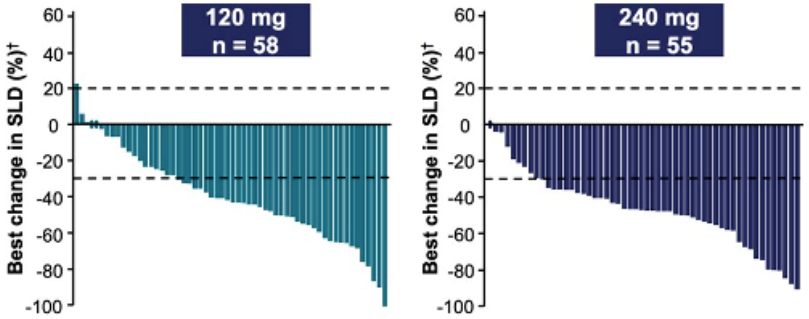

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Corassa M. ASCO 2025
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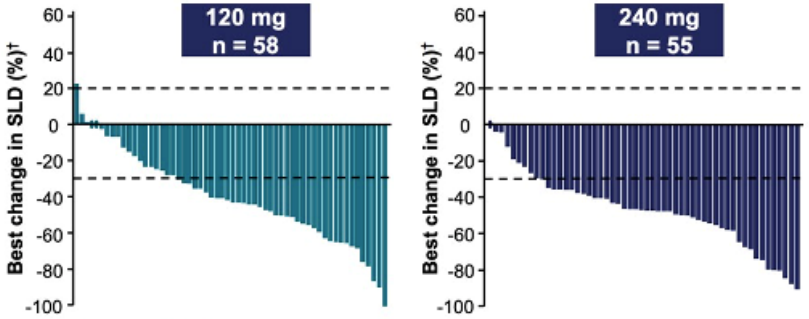

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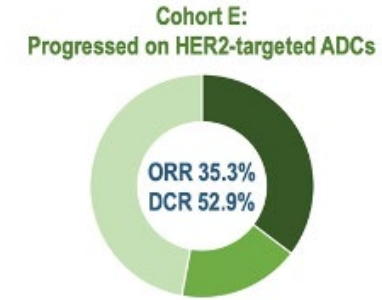
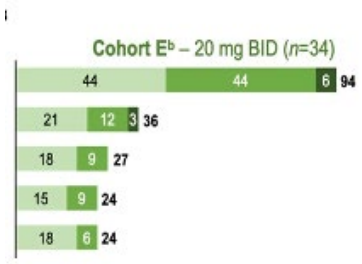
mPFS 12.9 months





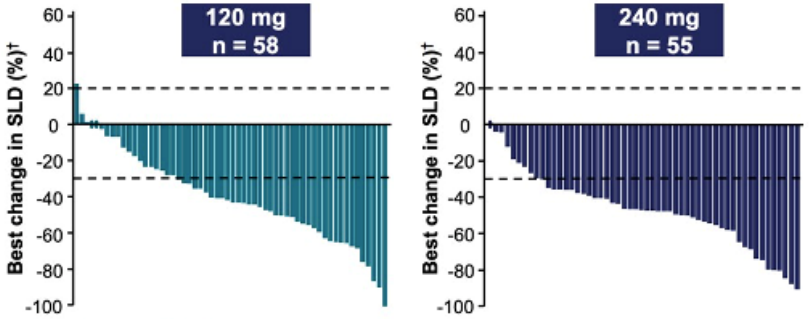
Corassa M. ASCO 2025
Heymatch GV. NEJM 2025

HER2

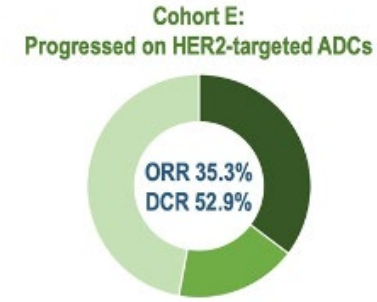
Oral Abstract 8504. SOHO-01: Safety and efficacy of BAY 2927088 (Sevabertinib)

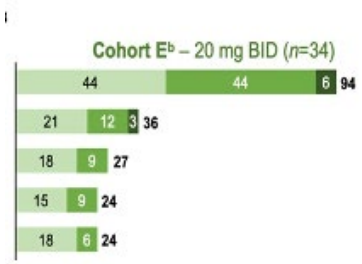
Alteration	Drug	Population	ORR	mDoR (months)	mPFS	mOS	FDA-Approved
HER2 mutations	T-Dxd	Pretreated	55%	9.3	8.2	17.3	Yes
	T-DM1	Pretreated/Naïve	44%	4.0	5.0	Not Available	No
	THP	Pretreated	29%	11.0	6.8	17.6	No
	Poziotinib	Pretreated/Naïve	27%	5.0	5.5	15.0	No
	Pyrotinib	Pretreated	30%	6.9	6.9	14.4	No
	Afatinib	Pretreated	13%	6.0	3.0	23.0	No

Beamion LUNG-1
Zongertinib



ORR 71%
mPFS 12.9 months





Drug	ILD G1	ILD ≥ G3
Sevabertinib	0%	0%
Zongertinib	0%	0%
T-Dxd 5.4 mg/kg	12.9%	2%

Corassa M. ASCO 2025
Heymatch GV. NEJM 2025

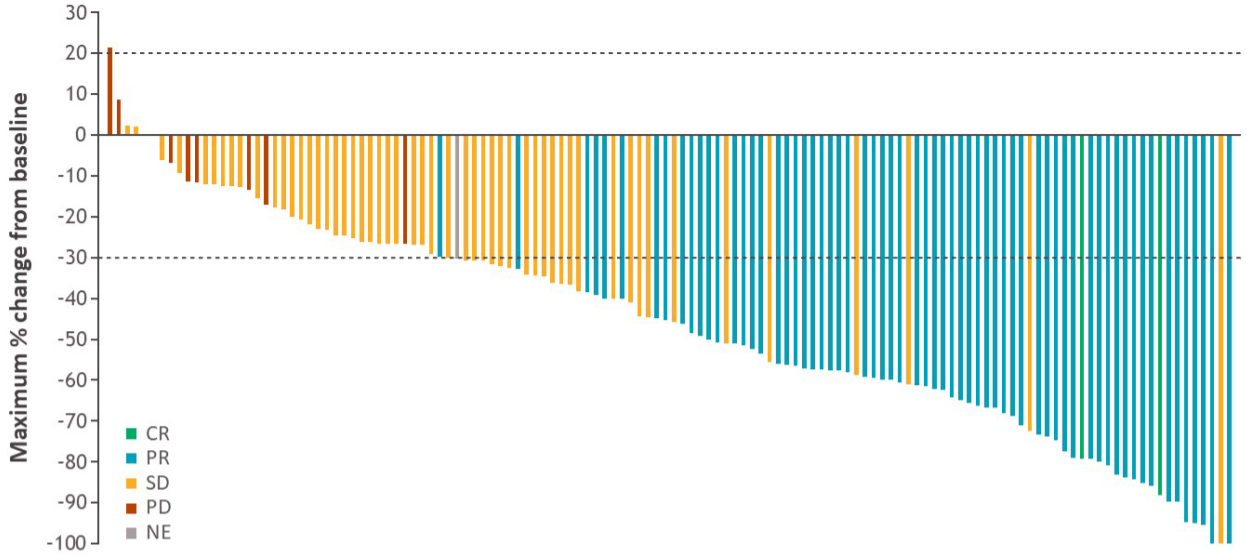
KRASG12C 1° linea

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

KRYSTAL-7: ADA + PEMBRO in 1L *KRAS*^{G12C} NSCLC

Response per investigator assessment in all patients

	All patients (N = 149)
ORR,[a] n (%)	66 (44)
95% CI	36-53
BOR, n (%)	
CR	2 (1)
PR	64 (43)
SD	55 (37)
PD	12 (8)
NE	16 (11)[b]
DCR,[c] n (%)	121 (81)
95% CI	74-87



- ORR in the biomarker-evaluable population was 36% (90% CI, 23-50) for PD-L1 TPS < 1%, 41% (90% CI, 25-58) for PD-L1 TPS 1-49%, and 61% (90% CI, 46-74) for PD-L1 TPS ≥ 50%

Waterfall plot includes evaluable patients with at least one target lesion at baseline and at least one post-baseline tumor assessment.
[a]ORR is defined as the proportion of patients with a confirmed CR/PR according to RECIST v1.1. [b]Reasons for no post-baseline imaging assessment were: non-treatment-related deaths (n = 5), withdrawal from the study (n = 2), non-compliant/lost to follow-up (n = 2), discontinuation due to TRAEs (n = 3) or non-TRAEs (n = 2), and global deterioration of health/clinical progression (n = 2). [c]DCR is defined as the proportion of patients with a confirmed CR/PR/SD according to RECIST v1.1.

- mDOR: 26m a nd the 12month DOR 73%

Garassino M JCO 2023

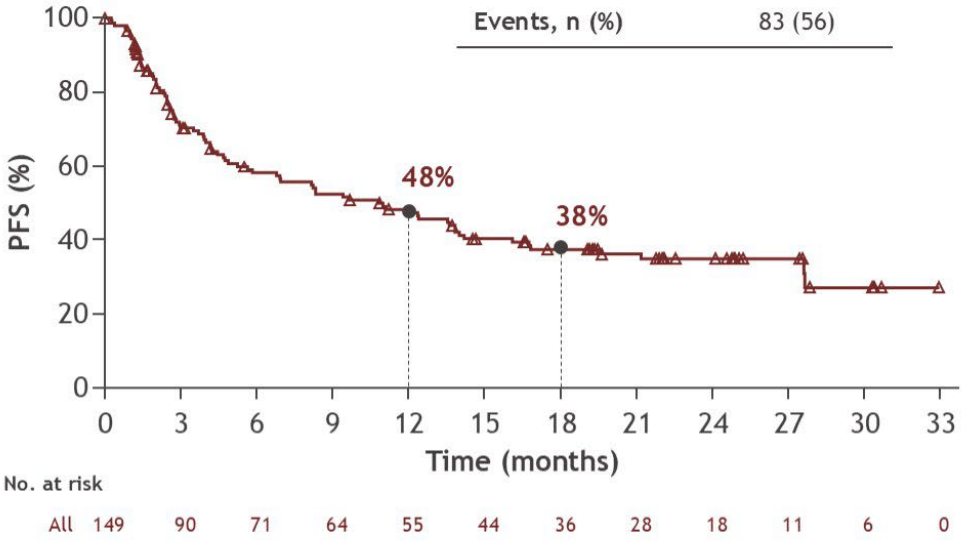
KRAS

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

KRYSTAL-7: ADA + PEMBRO in 1L *KRAS*^{G12C} NSCLC

PFS[a] and OS[b] in all patients

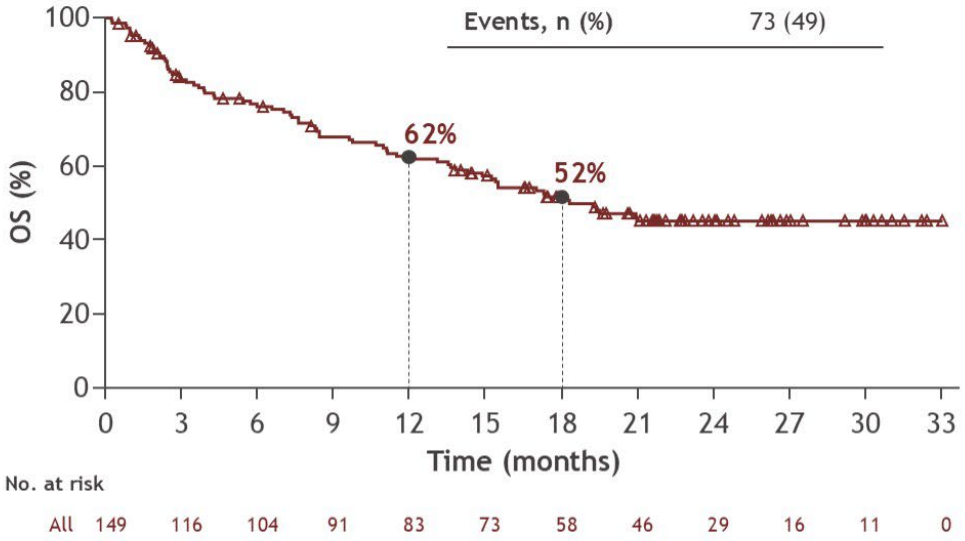
PFS	All patients (N = 149)
Median PFS, mo (95% CI)	11.0 (5.8-14.0)
Events, n (%)	83 (56)



No. at risk

All	149	90	71	64	55	44	36	28	18	11	6	0

OS	All patients (N = 149)
Median OS, mo (95% CI)	18.3 (14.3-NE)
Events, n (%)	73 (49)



No. at risk

All	149	116	104	91	83	73	58	46	29	16	11	0

- A total of 45 (30%) patients received subsequent anticancer therapy, the most common being chemotherapy (n = 21) and chemotherapy with checkpoint inhibitor therapy (n = 9)

Median follow-up: 22.8 mo.

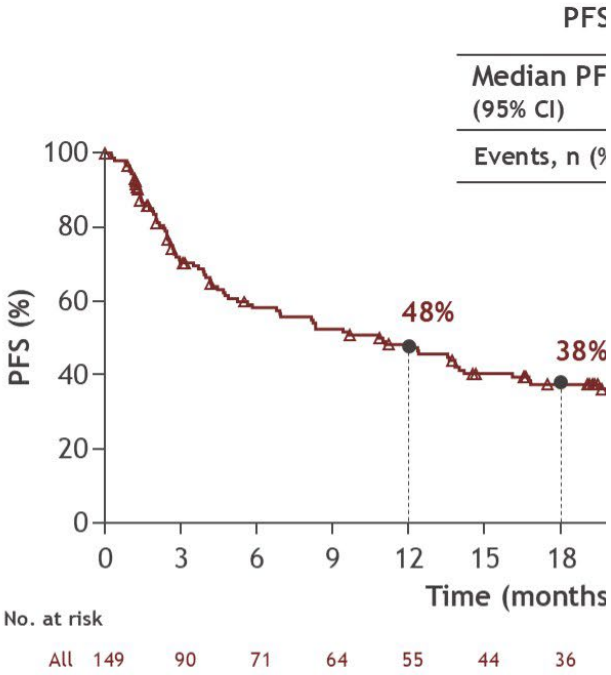
[a]PFS per investigator assessment. PFS is defined as the time from the date of first study treatment to the date of first PD or death due to any cause, whichever occurs first. [b]OS is defined as the time from the date of first study treatment to the date of death due to any cause.

KRAS

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

KRYSTAL-7: ADA + PEMBRO in 1L *KRAS*^{G12C} NSCLC

PFS[a] and OS[b] in all

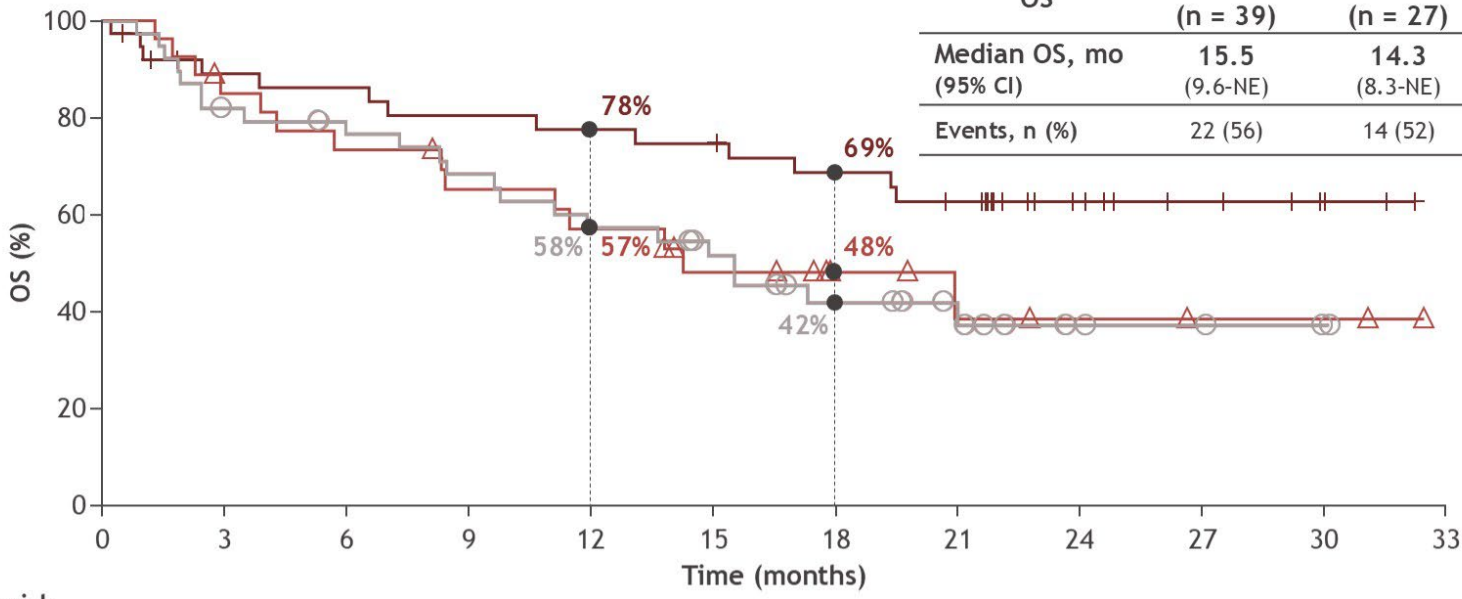


- A total of 45 (30%) patients receive chemotherapy with checkpoint inhi

Median follow-up: 22.8 mo.

[a]PFS per investigator assessment. PFS is defined as the time f time from the date of first study treatment to the date of de

OS according to PD-L1 status[a]



OS	PD-L1 < 1% (n = 39)	PD-L1 1-49% (n = 27)	PD-L1 ≥ 50% (n = 38)[b]
Median OS, mo (95% CI)	15.5 (9.6-NE)	14.3 (8.3-NE)	NR (19.4-NE)
Events, n (%)	22 (56)	14 (52)	13 (34)

No. at risk												
PD-L1 < 1%	39	31	28	25	21	17	12	8	4	3	1	0
PD-L1 1-49%	27	22	19	16	14	10	6	4	3	2	2	0
PD-L1 ≥ 50%	38	31	30	28	27	26	23	20	11	6	3	0

Median follow-up: 22.8 mo (all patients).

[a]OS in the biomarker-evaluable population. OS is defined as the time from the date of first study treatment to the date of death due to any cause. [b]Patients with PD-L1 TPS ≥ 50% included 18 patients with PD-L1 TPS 50-79% and 20 patients with PD-L1 TPS ≥ 80%.

KRAS

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

Toxicity

Patients, n (%)	PD-L1 < 50% (n = 95)	PD-L1 ≥ 50% (n = 54)	All patients (N = 149)
TRAEs			
Any grade	91 (96)	50 (93)	141 (95)
Grade 3	54 (57)	32 (59)	86 (58)
Grade 4	13 (14)	3 (6)	16 (11)
Grade 5	3 (3)	0	3 (2)[b]
TRAEs leading to			
ADA dose interruption	65 (68)	35 (65)	100 (67)
ADA dose reduction[c]	50 (53)	22 (41)	72 (48)
ADA discontinuation only	5 (5)	5 (9)	10 (7)
PEMBRO discontinuation only	19 (20)	6 (11)	25 (17)
ADA and PEMBRO discontinuation[d]	7 (7)	3 (6)	10 (7)
Any grade immune-related AEs	23 (24)	10 (19)	33 (22)

TRAEs G1-2 : Nausea, Diarrhea
iAEs: Pneumonitis 12%

Patients, n (%)	All patients (N = 149)				
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
Any hepatic TRAEs	**88 (59)**	**25 (17)**	**20 (13)**	**41 (28)**	**2 (1)**
Most frequent hepatic TRAEs[b]					
ALT increase	59 (40)	23 (15)	19 (13)	16 (11)	1 (< 1)
AST increase	53 (36)	20 (13)	12 (8)	19 (13)	2 (1)

KRAS

Oral Abstract 8500. KRYSTAL 7 Phase 2 . Adagrasib 400mg + Pembrolizumab all PDL1

Toxicity

Patients, n (%)	PD-L1 < 50% (n = 95)	PD-L1 ≥ 50% (n = 54)	All patients (N = 149)
TRAEs			
Any grade	91 (96)	50 (93)	141 (95)
Grade 3	54 (57)	32 (59)	86 (58)
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Any grade immune-related AEs	23 (24)	10 (19)	33 (22)

TRAEs G1-2 : Nausea, Diarrhea
iAEs: Pneumonitis 12%

Futuro: KRYSTAL 7 (en solo PDL1 > 50%)
KRYSTAL 4 + QT

Patients, n (%)	All patients (N = 149)				
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
Any hepatic TRAEs	**88 (59)**	**25 (17)**	**20 (13)**	**41 (28)**	**2 (1)**
Most frequent hepatic TRAEs[b]					
ALT increase	59 (40)	23 (15)	19 (13)	16 (11)	1 (< 1)
AST increase	53 (36)	20 (13)	12 (8)	19 (13)	2 (1)

KRASG12C 1° linea

Rapid oral Abstract 8519. Olomorasib + Pembrolizumab all PDL1 levels

Part G: 1L NSCLC
Olomorasib + pembrolizumab[a]
Randomized 1:1[b]
(n=43)

Part G Eligibility

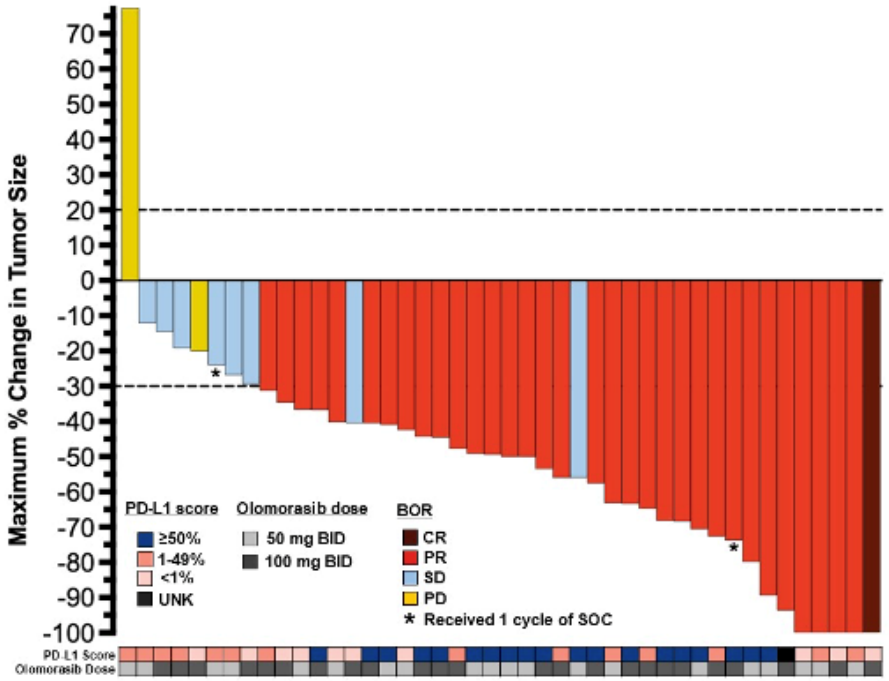
- No prior therapy for metastatic disease[c]
- All PD-L1 expression permitted

Key objectives

- Safety and Tolerability
- Determine MTD and R2PD
- Pharmacokinetics
- ORR, DCR, PFS and DoR per RECIST v1.1

Efficacy of 1L Olomorasib + Pembrolizumab

ORR 90% PDL1 50%



	Olomorasib + Pembrolizumab	
Efficacy Evaluable Patients[a]	**All n=46**	**PD-L1 ≥50% n=20**
BOR, n (%)		
CR	1 (2)	0 (0)
PR	33 (72)	18 (90)
SD	8 (17)	1 (5)
PD	3 (7)[b]	1 (5)[b]
NE	1 (2)	0 (0)
ORR, % (95% CI)[c]	**74 (58.9-85.7)**	**90 (68.3-98.8)**
DCR, % (95% CI)	91 (79.2-97.6)	95 (75.1-99.9)
Median DOR, months (95% CI)	NE (10.5-NE)	NE (10.5-NE)
Median PFS, months (95% CI)	NE (12.0-NE)	NE (12.0-NE)
6-month PFS rate, % (95% CI)	80.2 (64.1-89.6)	89.7 (64.8-97.3)
12-month PFS rate, % (95% CI)	66.7 (40.9-83.2)	59.8 (8.2-90.0)

KRASG12C 1° linea

Rapid oral Abstract 8519. Olomorasib Pembrolizumab all PDL1 levels

GECP lung cancer research

Part G: 1L NSCLC
Olomorasib + pembrolizumab[a]
Randomized 1:1[b]
(n=43)

Part G Eligibility

- No prior therapy for metastatic disease[c]
- All PD-L1 expression permitted

Key objectives

- Safety and Tolerability
- Determine MTD and R2PD
- Pharmacokinetics
- ORR, DCR, PFS and DoR per RECIST v1.1

Safety Profile: 1L Olomorasib + Pembrolizumab

Olomorasib (50 or 100 mg BID) + Pembrolizumab (n=48)							
Parameter n (%)	TEAEs (≥10%)		TRAEs[a]				
	Any Grade	Grade ≥ 3	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4[b]
Any AE	45 (93.8)	26 (54.2)	43 (89.6)	9 (18.8)	15 (31.3)	17 (35.4)	2 (4.2)
Diarrhea	20 (41.7)	4 (8.3)	17 (35.4)	8 (16.7)	5 (10.4)	4 (8.3)	-
ALT increased	16 (33.3)	11 (22.9)	14 (29.2)	1 (2.1)	2 (4.2)	11 (22.9)	-
AST increased	14 (29.2)	7 (14.6)	14 (29.2)	2 (4.2)	5 (10.4)	7 (14.6)	-
Nausea	13 (27.1)	-	9 (18.8)	6 (12.5)	3 (6.3)	-	-
Fatigue	11 (22.9)	-	7 (14.6)	2 (4.2)	5 (10.4)	-	-
Vomiting	10 (20.8)	-	6 (12.5)	3 (6.3)	3 (6.3)	-	-
Decreased appetite	8 (16.7)	1 (2.1)	6 (12.5)	4 (8.3)	2 (4.2)	-	-
Pruritis	9 (18.8)	-	7 (14.6)	6 (12.5)	1 (2.1)	-	-
Abdominal pain	9 (18.8)	-	3 (6.3)	2 (4.2)	1 (2.1)	-	-
Peripheral oedema	8 (16.7)	1 (2.1)	2 (4.3)	-	-	-	-
Constipation	7 (14.6)	1 (2.1)	1 (2.1)	1 (2.1)	-	-	-

Dose modifications due to TRAEs

TRAEs led to dose reductions of olomorasib in 11 patients (23%)

TRAEs[c] led to discontinuation of the treatment regimen in 2 patients (4%)

KRAS G12C 2º linea

Rapid oral Abstract. Phase II Sosimerasib 500mg. (china)

Efficacy ORR

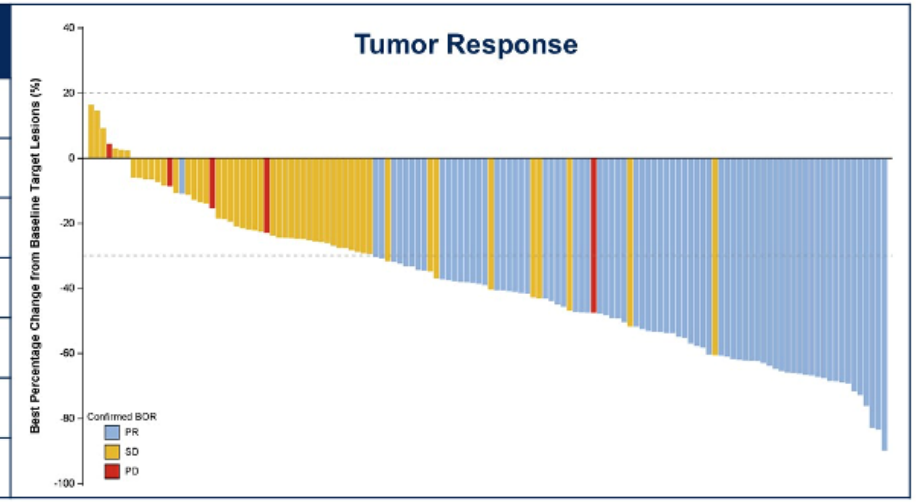
KRAS G12C 2º linea

Rapid oral Abstract. Phase II Sosimerasib 500mg. (china)

Efficacy ORR

ORR

Response (IRC)	N=145
Median follow-up, months	6.8
Confirmed BOR, n (%)	
PR	76 (52.4)
SD	51 (35.2)
Non-CR/Non-PD	8 (5.5)
PD	5 (3.4)
Confirmed ORR (95% CI)	52.4 (44.0-60.8)



Cut-off date: November 3, 2024

KRAS G12C 2º linea

Rapid oral Abstract. Phase II Sosimerasib 500mg. (china)

Efficacy ORR

ORR

Response (IRC)	N=145
Median follow-up, months	6.8
Confirmed BOR, n (%)	
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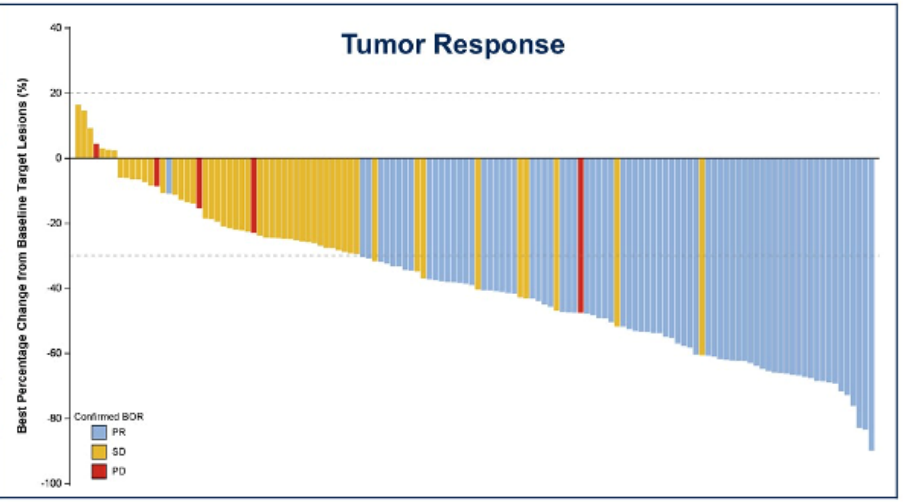
PD	5 (3.4)
Confirmed ORR (95% CI)	52.4 (44.0-60.8)



Cut-off date: November 3, 2024

Response (IRC)	N=145
Median follow-up, months	6.8
DCR (95% CI)	87.6 (81.1-92.5)
TTR	
Median (range), months	1.4 (1.2-8.4)
DOR	
Median (95% CI), months	NA (5.4-NA)
PFS	
Events, n (%)	62 (42.8)
Median (95% CI), months	7.2 (5.6-NA)
6-month PFS rate (95% CI)	56.7 (47.5-65.0)
OS	
Deaths, n (%)	31 (21.4)
Median (95% CI), months	NA (NA-NA)
6-month OS rate (95% CI)	86.6 (79.8-91.3)

Cut-off date: November 3, 2024

KRAS G12C 2º linea

Rapid oral Abstract. Phase II Sosimerasib 500mg. (china)

Efficacy ORR

ORR

Response (IRC)	N=145
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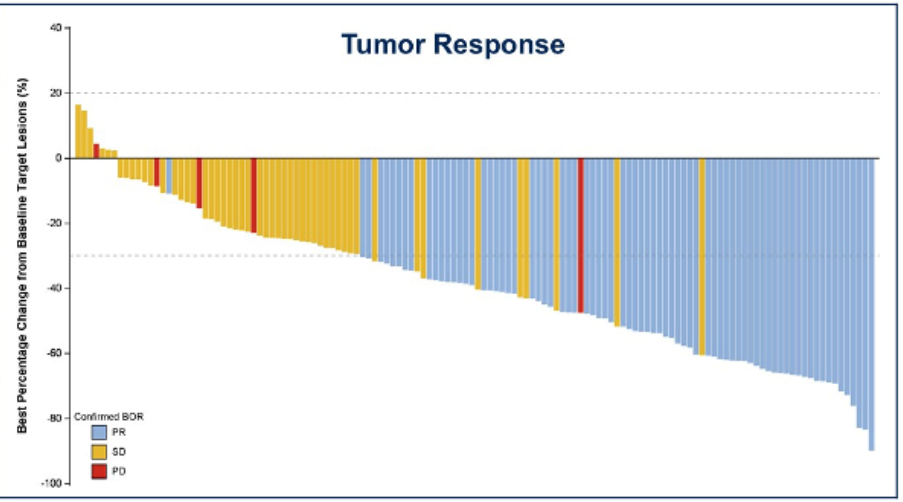


Cut-off date: November 3, 2024

Response (IRC)	N=145
Median follow-up, months	6.8
DCR (95% CI)	87.6 (81.1-92.5)
TTR	
Median (range), months	1.4 (1.2-8.4)
DOR	
Median (95% CI), months	NA (5.4-NA)
PFS	
Events, n (%)	62 (42.8)
Median (95% CI), months	7.2 (5.6-NA)
6-month PFS rate (95% CI)	56.7 (47.5-65.0)
OS	
Deaths, n (%)	31 (21.4)
Median (95% CI), months	NA (NA-NA)
6-month OS rate (95% CI)	86.6 (79.8-91.3)

Cut-off date: November 3, 2024

Common TRAEs	Any Grade	Grade ≥ 3
ALT increased	66.2%	9.0%
AST increased	62.8%	9.0%
Anemia	31.7%	3.4%
GGT increased	26.2%	15.2%
ALP increased	22.1%	6.9%
Nausea	17.9%	0

KRASG12C 2º línea

Rapid Oral Abstract 8518. LUNG MAP. Impact of comutations

Lung-MAP S1900E Schema

LUNGMAP Master Protocol

KRAS G12C mutation identified by FoundationOne® CDx tissue assay

Lung-MAP S1900E

- Recurrent or metastatic *KRAS* G12C non-squamous NSCLC
- ECOG PS 0-1
- Received at least one prior systemic therapy
- No uncontrolled brain metastasis

- Cohort 1 [a]: *TP53*^{MUT} Target N=40
- Cohort 2 [b]: *STK11*^{MUT} Target N=25
- Cohort 3 [c]: OTHER^{MUT} Target N=36

Sotorasib 960 mg QD → End of Treatment → Long-term Follow Up

Primary Endpoint: Response by RECIST 1.1*
Secondary Endpoints: Duration of response, Progression free survival, Overall survival, Toxicity

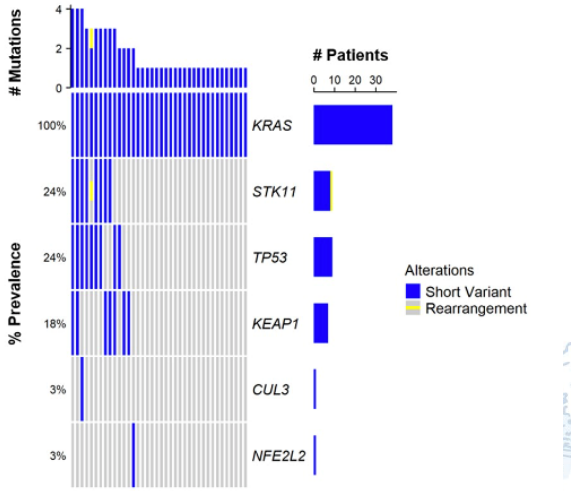
Treatme
- Sotorasib until progression, int
- Imaging every 6 weeks
- ctDNA baseline, C2D1, C3D1, a

Mutation spectrum in OTHER co-mut cohort

9 (24%) tumors with KEAP1, NFE2L2, or CUL3 co-mut

Co-Mutation Spectrum	N (%)*
No Co-Mutation in Protocol-Defined Biomarkers	**24 (63)**
Triple Co-Mutations (Total)	**3 (8)**
• *TP53/STK11/KEAP 1*	2
• *TP53/STK11/CUL3*	1
Double Co-Mutations (Total)	**7 (18)**
• *TP53/STK11*	4
• *STK11/KEAP1*	2
• *TP53/KEAP1*	1
Single Co-Mutation (Total)	**3 (8)**
• *KEAP1*	2
• *NFE2L2*	1

*One pt in cohort 3 with only known *TP53* co-mutation as tumor purity low and unable to confirm wild type status of other genes

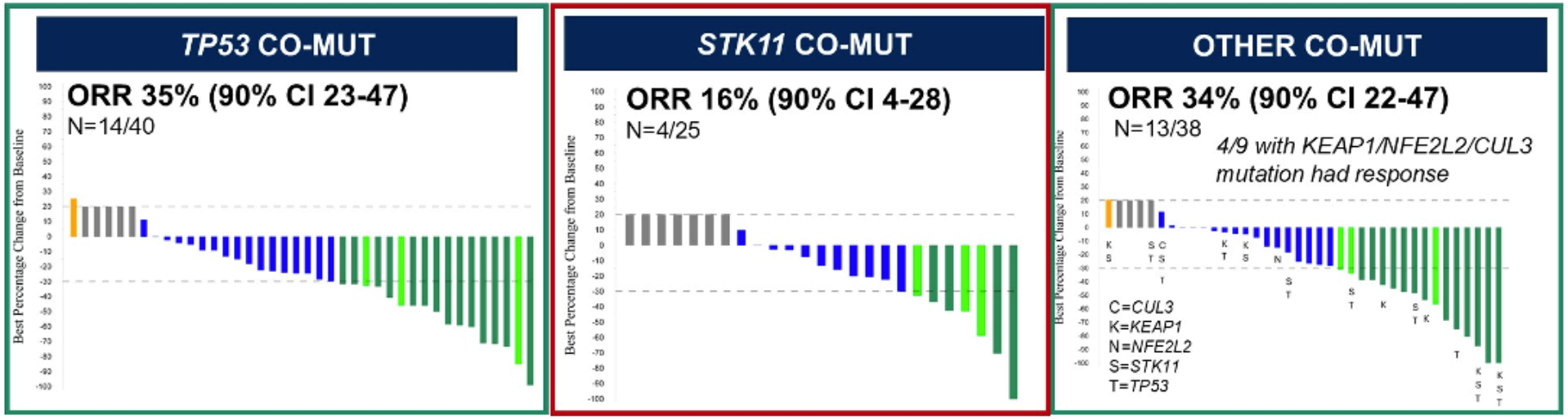


KRASG12C 2º línea

Rapid Oral Abstract 8518. LUNG MAP. Impact of comutations

Lung-MAP S1900E Primary Endpoint Objective Response Rate:

TP53 and OTHER co-mut met primary endpoint while STK11 co-mut did not



	TP53 CO-MUT	*STK11* CO-MUT	OTHER CO-MUT
DCR (90% CI)	78% (67-88); N=31/40	60% (44-76); N=15/25	79% (68-90); N=30/38
Median DOR (95% CI)	7.1 mo (2.7-11.5)	7.9 mo (1.6-NA)	6.8 mo (3.0-11.8)

KRASG12C 2º línea

Rapid Oral Abstract 8518. LUNG MAP. Impact of comutations

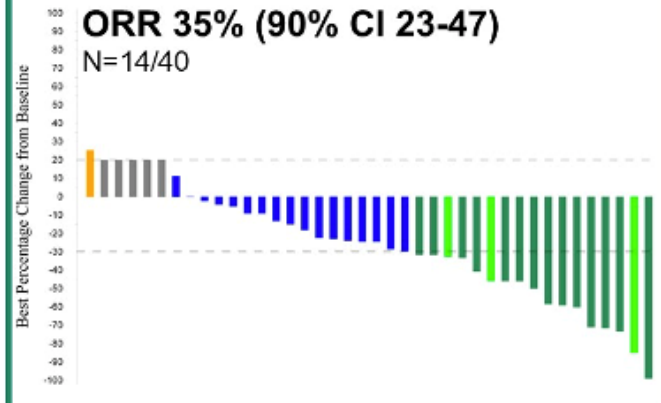
Lung-MAP S1900E Primary Endpoint Objective Response Rate:

TP53 and OTHER co-mut met primary endpoint while STK11 co-mut did not

TP53 CO-MUT

ORR 35% (90% CI 23-47)

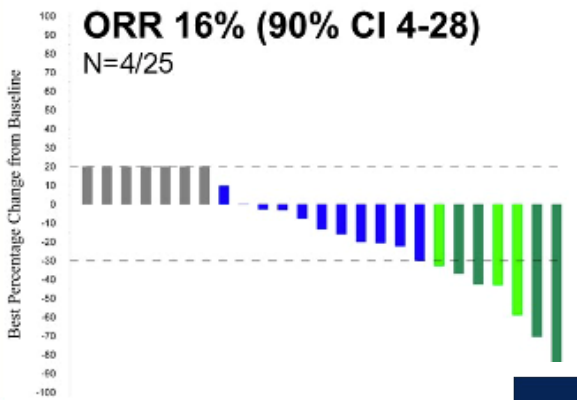
N=14/40



STK11 CO-MUT

ORR 16% (90% CI 4-28)

N=4/25

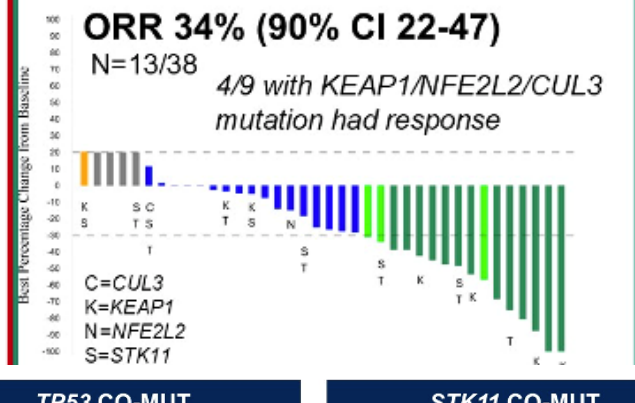


OTHER CO-MUT

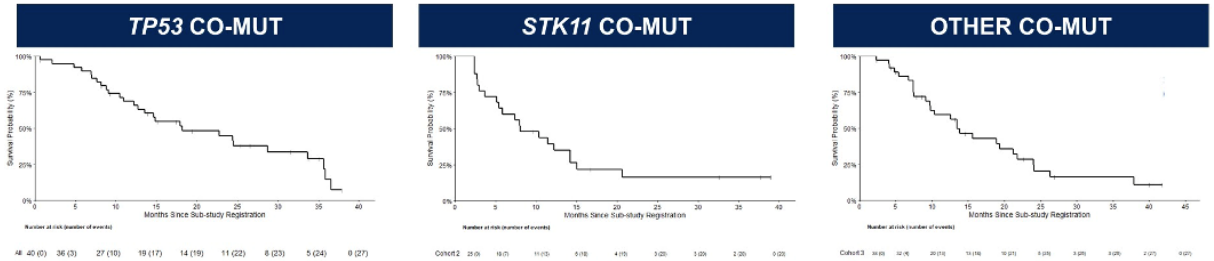
ORR 34% (90% CI 22-47)

N=13/38

4/9 with KEAP1/NFE2L2/CUL3 mutation had response



	TP53 CO-MUT	*STK11* CO-MUT	OTHER CO-MUT
DCR (90% CI)	78% (67-88); N=31/40	60% (44-76); N=15/25	
Median DOR (95% CI)	7.1 mo (2.7-11.5)	7.9 mo (1.6-NA)	



	TP53 CO-MUT	*STK11* CO-MUT	OTHER CO-MUT
Median OS (95% CI)	**18.2** mo (12.2-33.7)	**8.0** mo (5.1-14.2)	**13.5** mo (9.7-21.2)
6 mo OS	90%	60%	86%
12 mo OS	69%	39%	59%

KRASG12 C

Poster Abstract MK 1084. Phase I KANDLELI 001

Figure 1. KANDLELIT-001 study design. KANDLELIT-001 is an ongoing, open-label, phase 1 study of the KRAS G12C inhibitor MK-1084 that is being conducted at 68 global sites. Dose escalation followed a modified toxicity probability interval design; optional dose expansion cohorts were prespecified.

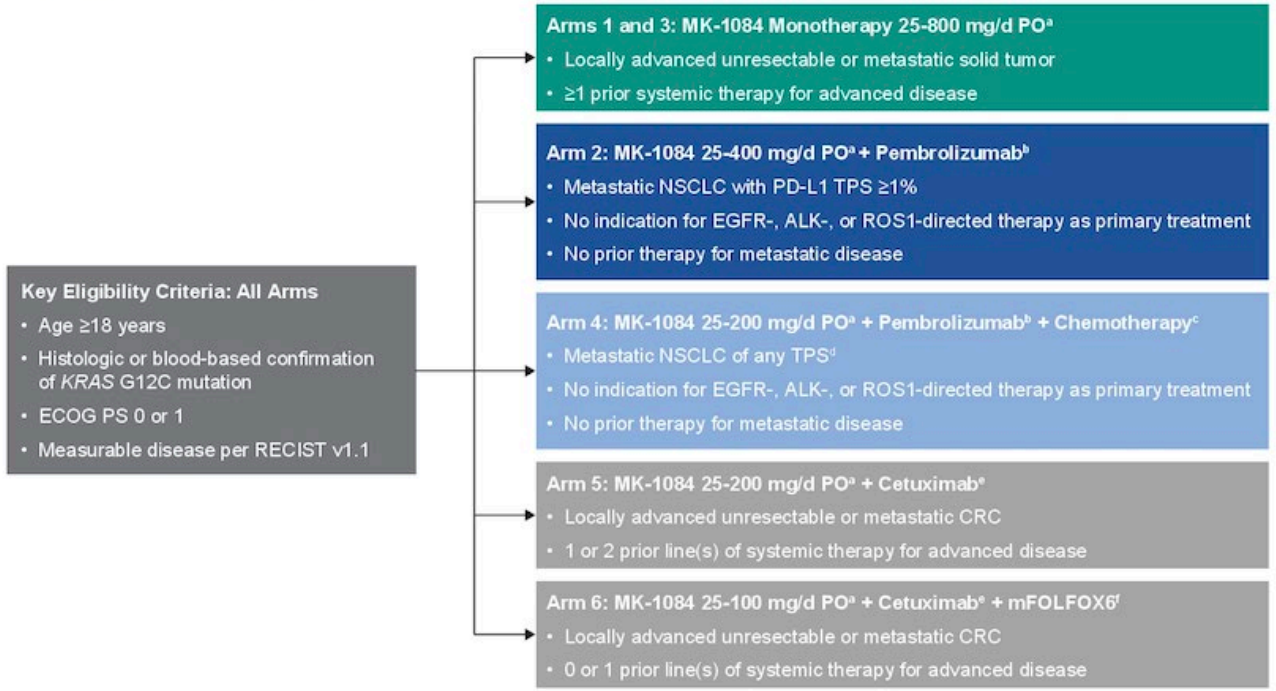
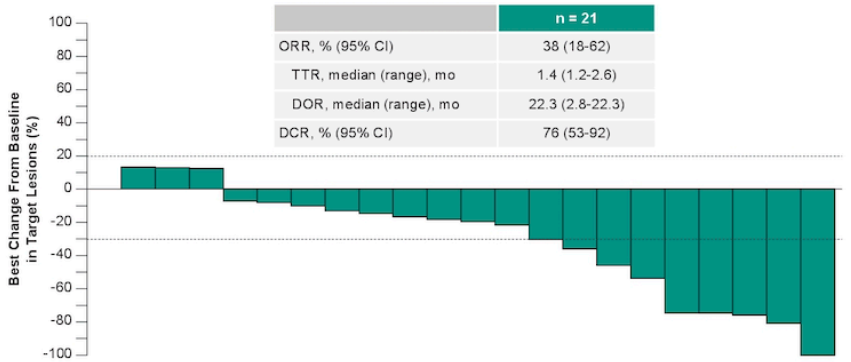


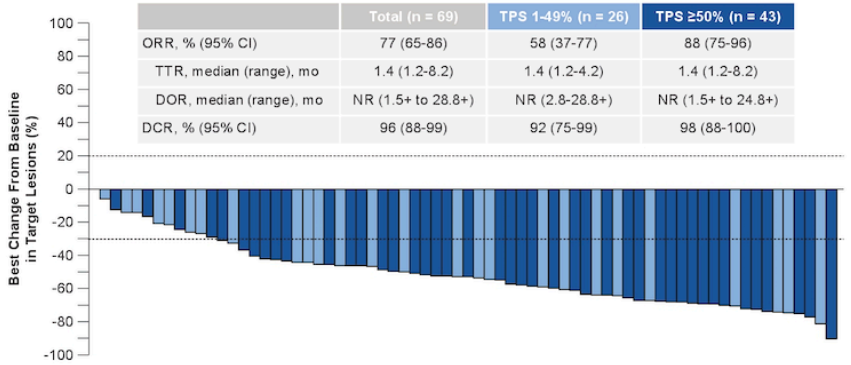
Figure 4. Antitumor activity assessed per RECIST v1.1 by investigator review in participants with NSCLC (efficacy population)

Arms 1 + 3: MK-1084 monotherapy (previously treated NSCLC only)



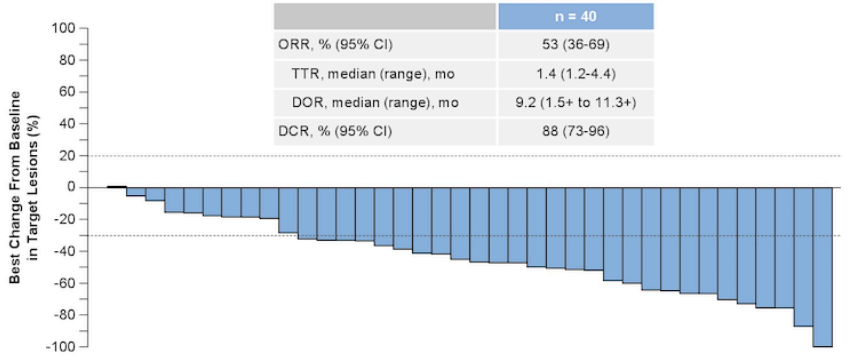
	n = 21
ORR, % (95% CI)	38 (18-62)
TTR, median (range), mo	1.4 (1.2-2.6)
DOR, median (range), mo	22.3 (2.8-22.3)
DCR, % (95% CI)	76 (53-92)

Arm 2: MK-1084 + pembrolizumab (1L NSCLC with TPS ≥1%)



	Total (n = 69)	TPS 1-49% (n = 26)	TPS ≥50% (n = 43)
ORR, % (95% CI)	77 (65-86)	58 (37-77)	88 (75-96)
TTR, median (range), mo	1.4 (1.2-8.2)	1.4 (1.2-4.2)	1.4 (1.2-8.2)
DOR, median (range), mo	NR (1.5+ to 28.8+)	NR (2.8-28.8+)	NR (1.5+ to 24.8+)
DCR, % (95% CI)	96 (88-99)	92 (75-99)	98 (88-100)

Arm 4: MK-1084 + pembrolizumab + chemotherapy (1L NSCLC)

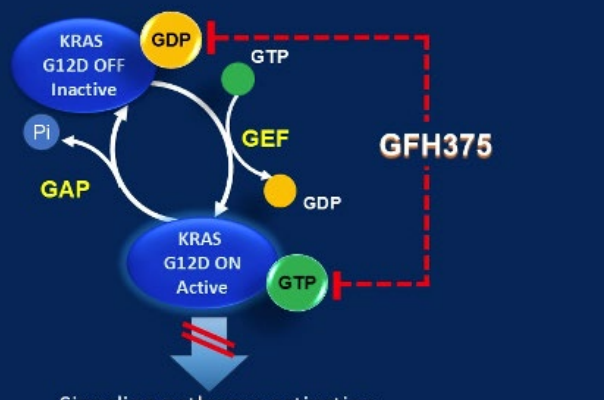


	n = 40
ORR, % (95% CI)	53 (36-69)
TTR, median (range), mo	1.4 (1.2-4.4)
DOR, median (range), mo	9.2 (1.5+ to 11.3+)
DCR, % (95% CI)	88 (73-96)

KRASG12D

Abstract. GFH 375 Phase I and II

- GFH375 is a highly selective and potent KRAS G12D inhibitor targeting both the “ON” (GTP-bound) and “OFF” (GDP-bound) states.



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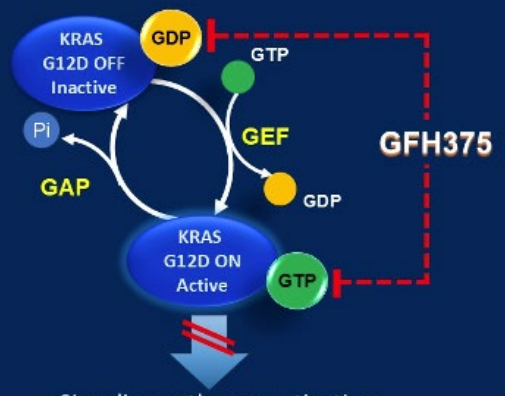

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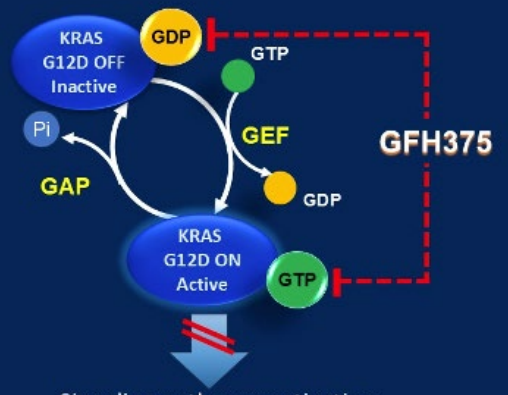
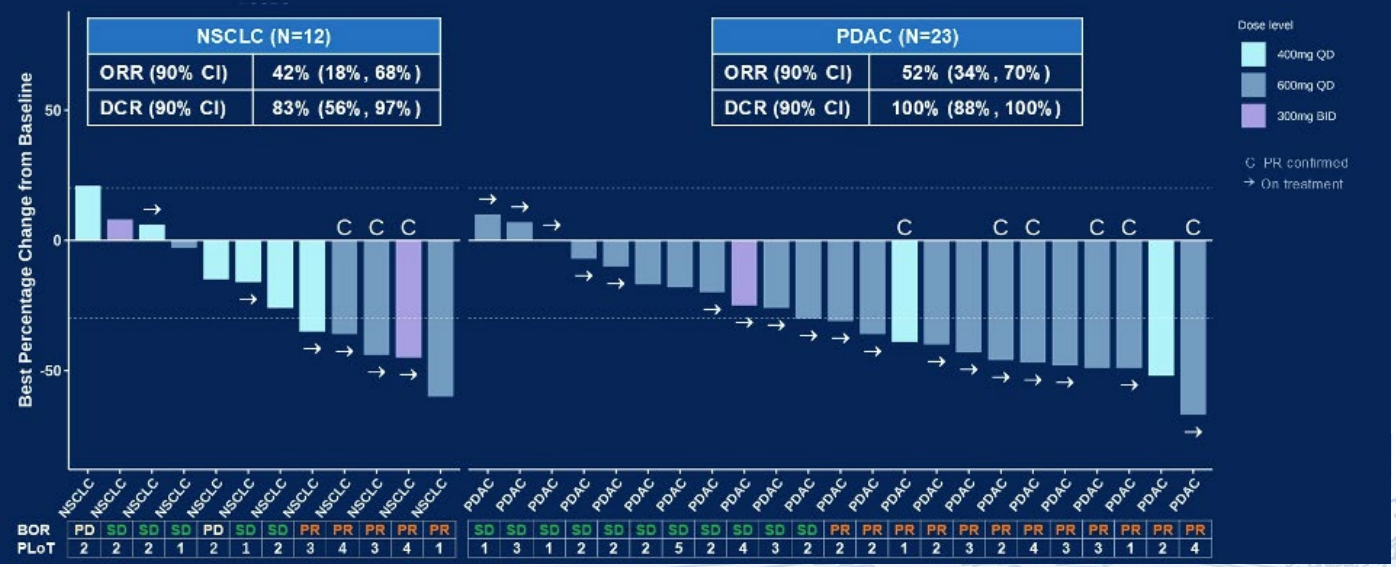


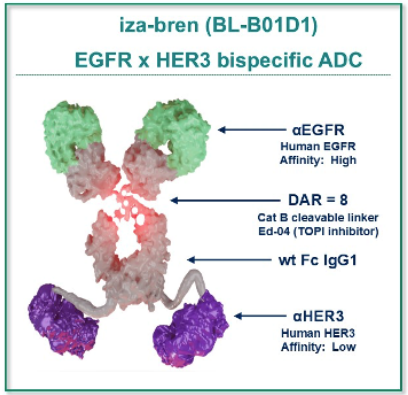
Efficacy in NSCLC and PDAC Patients at Target Dose Range

- 12 NSCLC and 23 PDAC patients treated at 400 mg QD, 600 mg QD or 300 mg BID had tumor response assessed.*

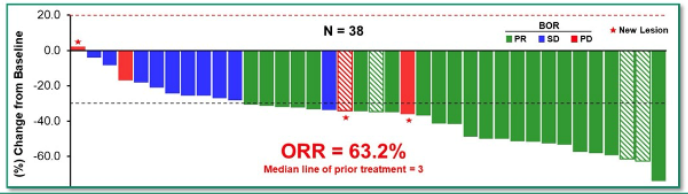


Multdriver

Rapid oral Abstract 3001 . Phase I Iza- bren (BL01D1) ADC EGFRxHER3



- iza-bren (izalontamab brengitecan) is a potential first-in-class ADC comprised of an **EGFR x HER3 bispecific antibody** conjugated to a novel topo-I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker.
- In the previous phase I trial, iza-bren showed promising anti-tumor activity in **EGFRmut NSCLC patients (63.2% ORR)†**.



The safety and preliminary efficacy of iza-bren in NSCLC patients with **driver genomic alterations outside of classic EGFR mutations** was evaluated in this phase Ib study.

Multdriver

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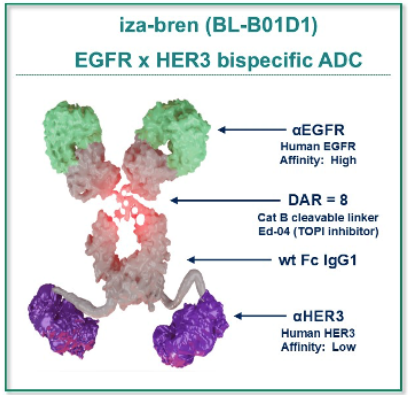

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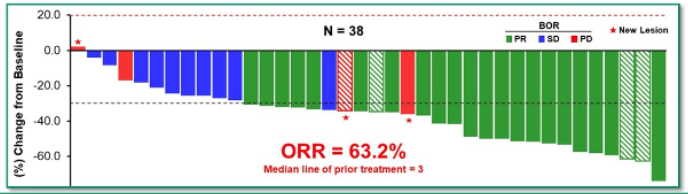

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- Locally advanced or metastatic NSCLC
- Presence of driver genomic alterations outside of classic EGFR mutations (19del and L858R)
- ECOG PS 0-1
- Measurable disease per RECIST v1.1
- Failed standard treatment
- Received no more than one prior line of chemotherapy

Treatment

iza-bren
2.5 mg/kg
D1D8 Q3W

Endpoints

Primary
- Safety

Secondary
- ORR, DCR and DoR

Exploratory
- PFS and OS

Multdriver

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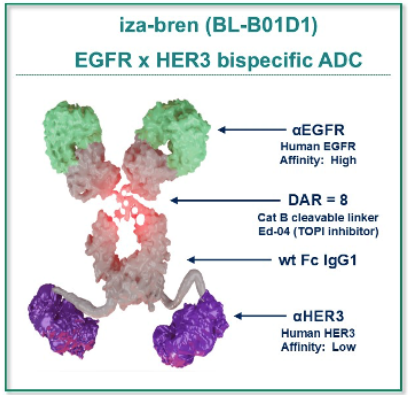

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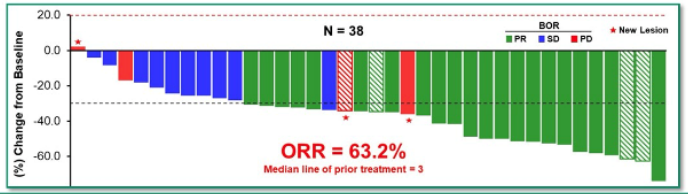

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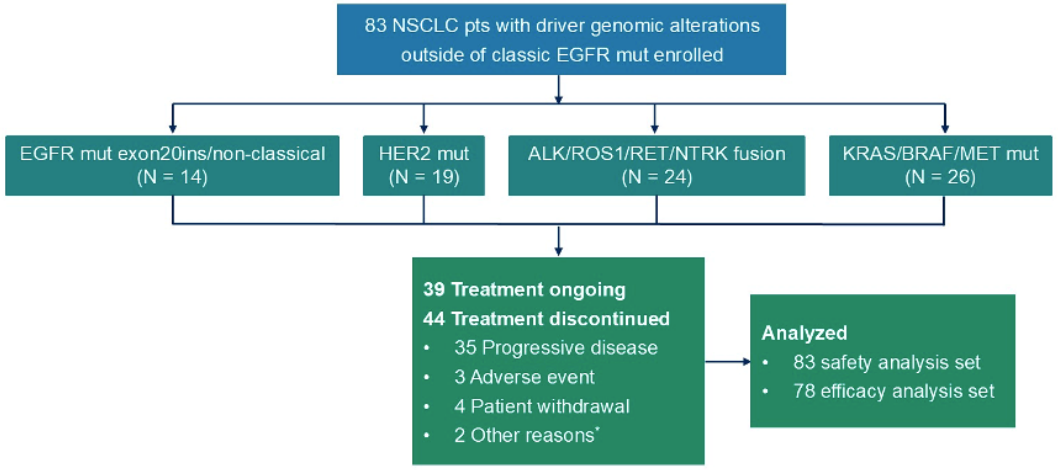

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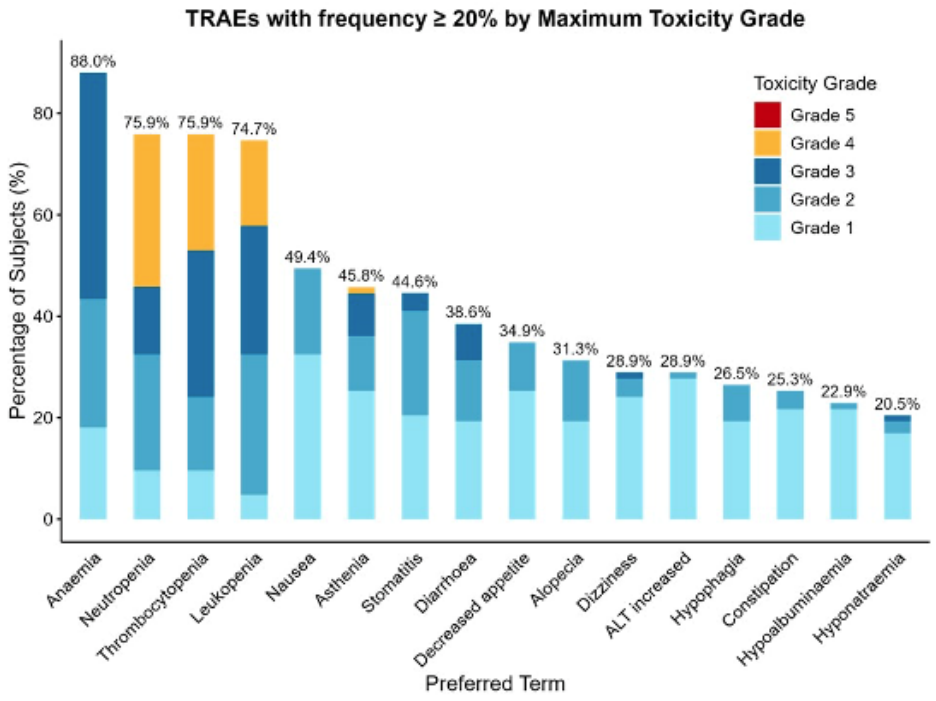

Multidriver

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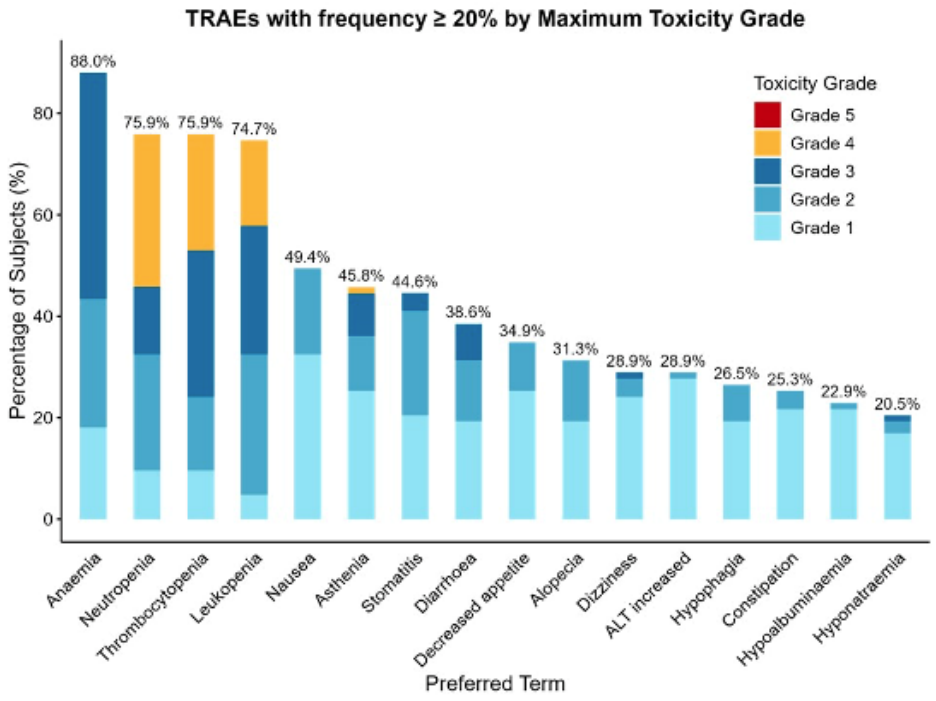

Solo 1 caso ILD

Multidriver

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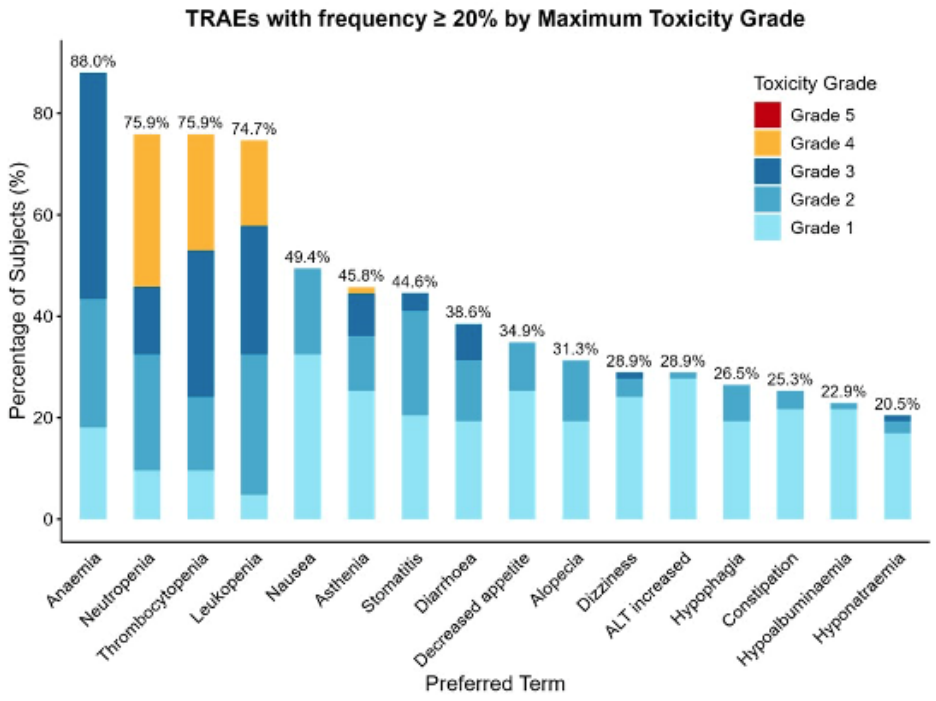
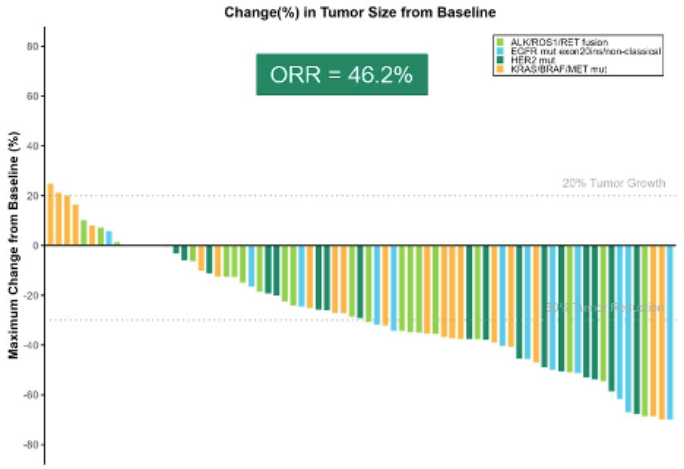
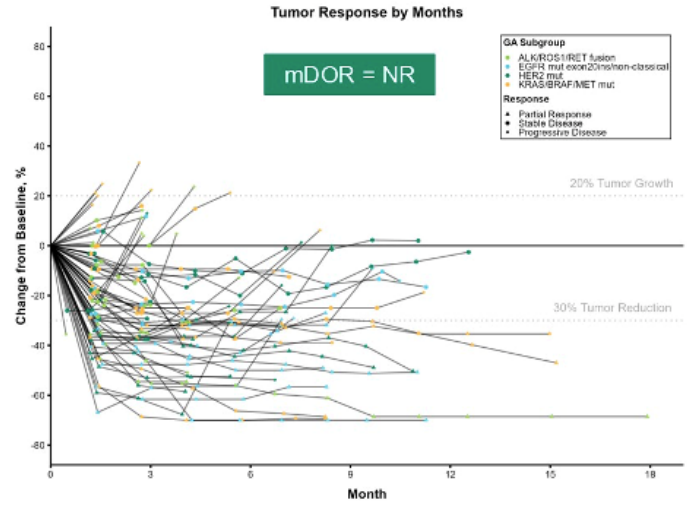




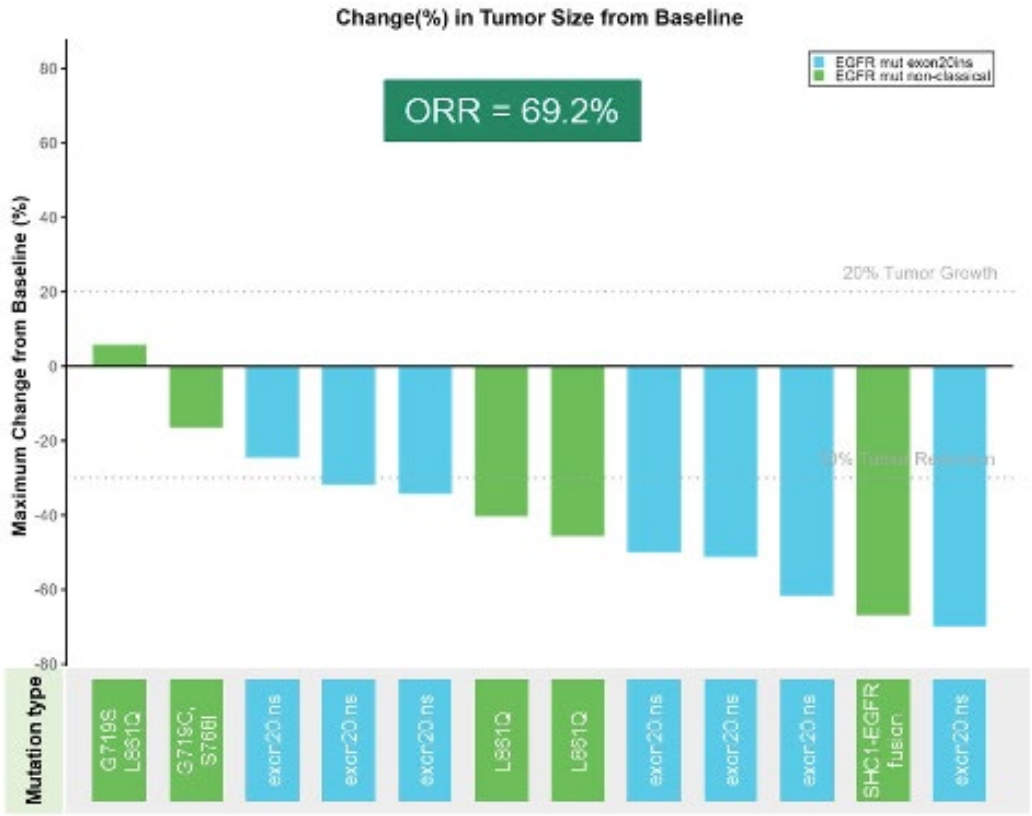


81.3% of patients with tumor shrinkage and the median (range) shrinkage (%) was -29.2 (-70.1, 24.9).

Solo 1 caso ILD

Multidriver

Abstract. Izabren BL01D1



Multidriver

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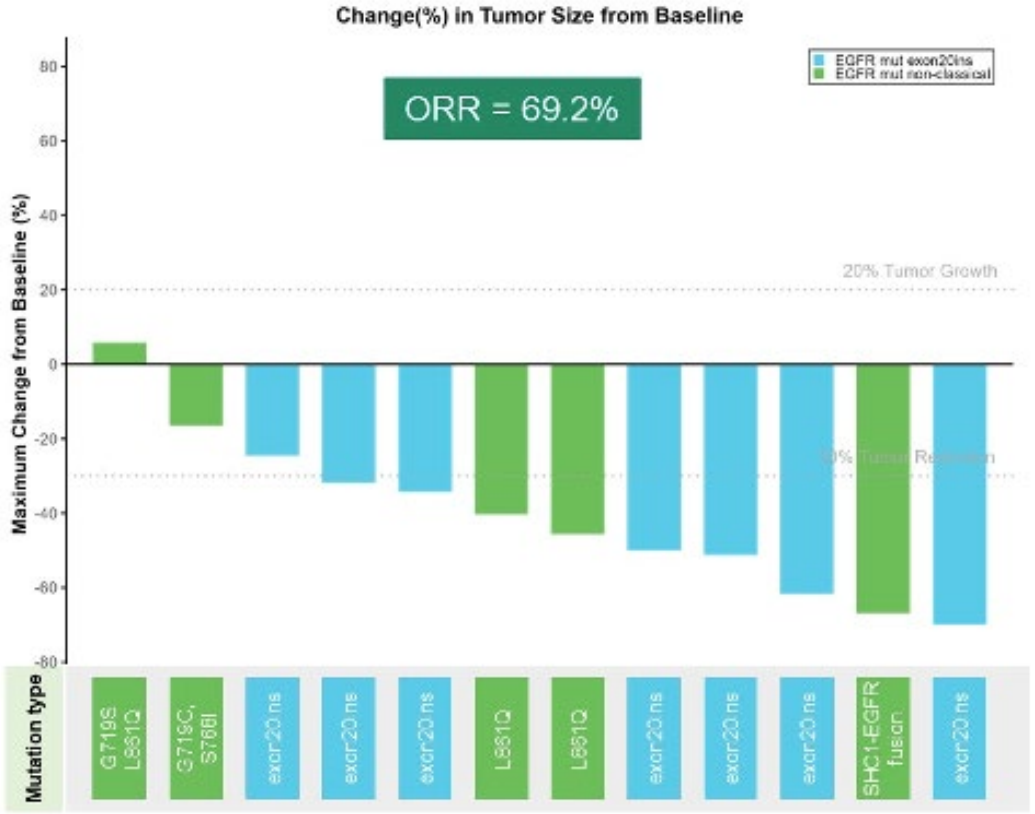
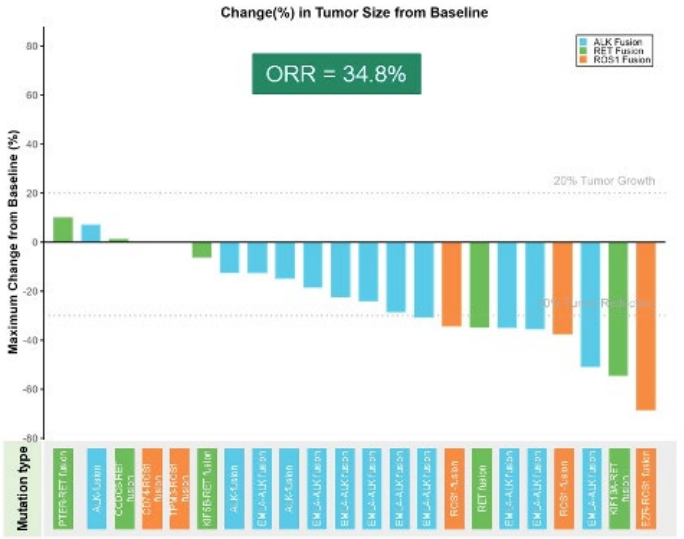


ALK/ROS1/RET fusion



GECP lung cancer research

Multidriver

Abstract. Izabren BL01D1

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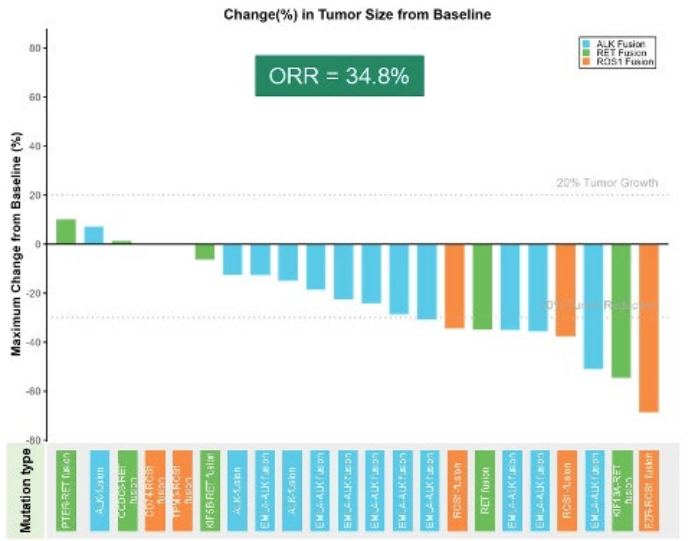
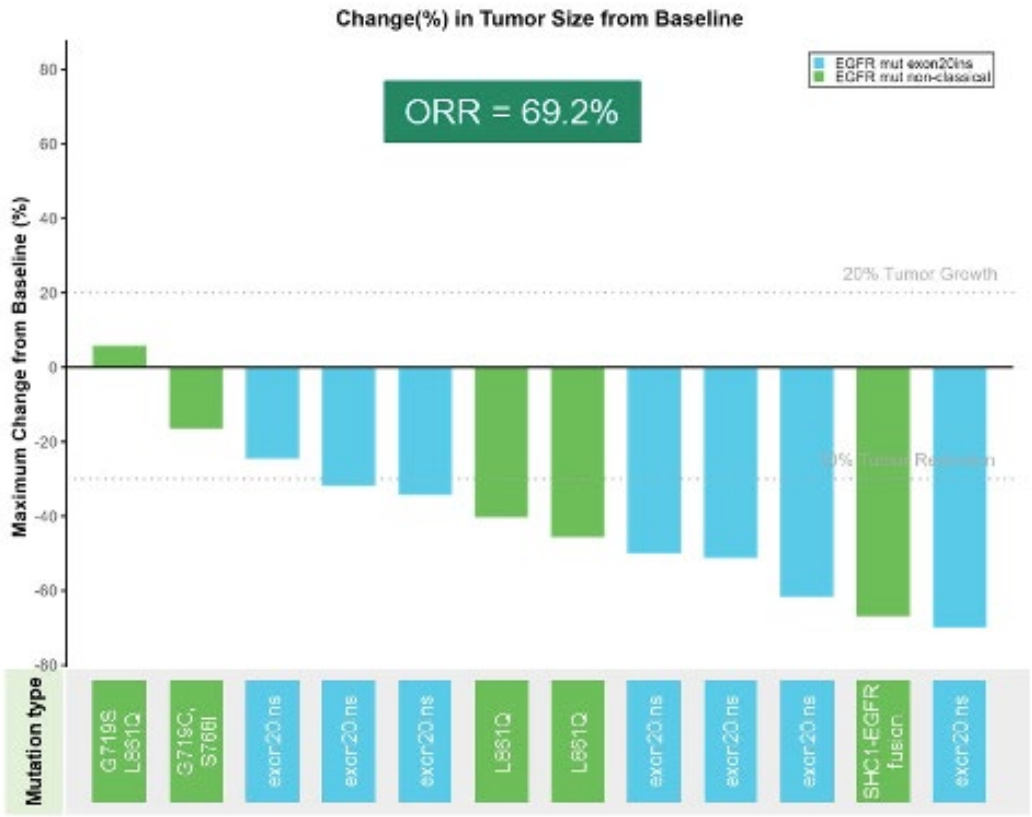
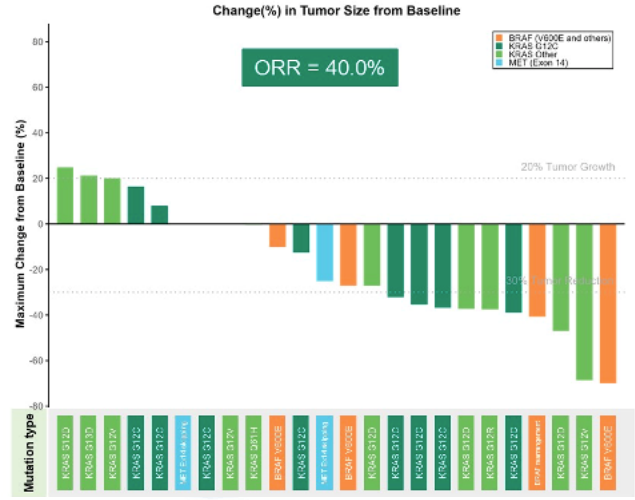




KRAS/BRAF/MET mut



Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Iniciativa científica de:
GECP lung cancer research

Enfermedad avanzada dirigidos a diana. Conclusiones

Mónica Antoñanzas Basa

Hospital Clínico San Carlos