Novedades & Claves en CÁNCER de PULMÓN 2023

Enfermedad metastásica

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Con la colaboración de:

Bristol Myers Squibb™

Janssen Oncology

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Organizado por:

GECP lung cancer research

ÍNDICE

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ÍNDICE

1. **Novedades para pacientes sin diana accionable**
    - Inmunoterapia
    - No inmunoterapia
2. **Novedades para pacientes con diana accionable**
    - EGFR
        i. 1ª línea
        ii. 2ª línea
        iii. Mutaciones infrecuentes
    - MET
    - RET
    - BRAF

El pastel importante !!!

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Novedades para pacientes sin diana accionable

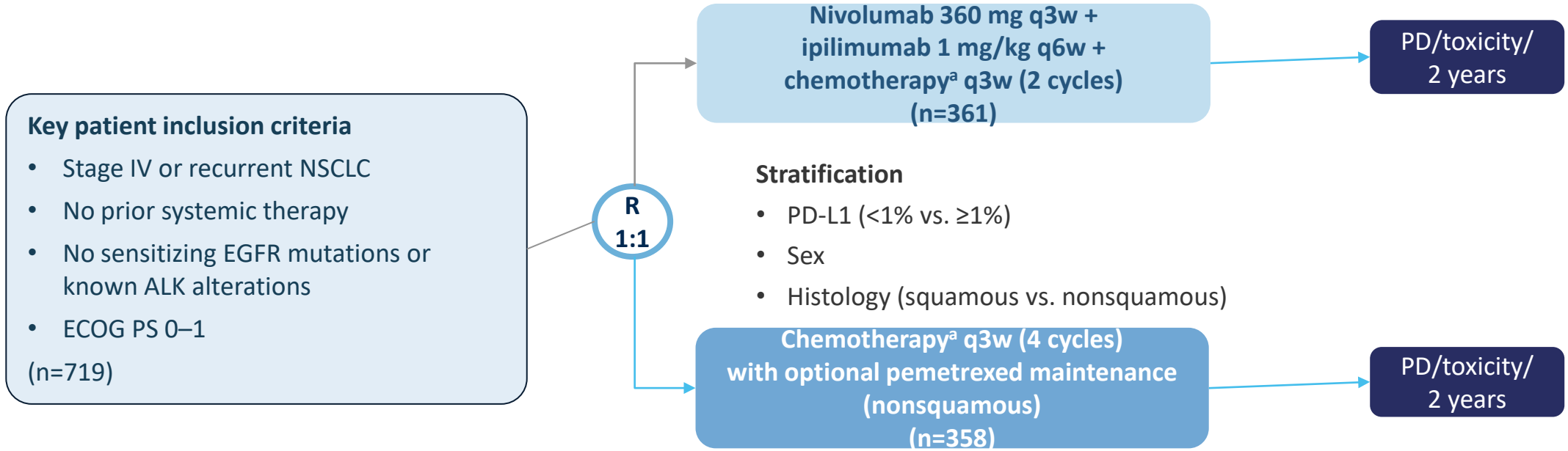
INMUNOTERAPIA

- Actualización a 4 años y por subtipo del estudio Checkmate 9LA (ASCO)

- Ensayo PERLA: **Dostarlimab** + quimioteràpia vs Pembrolizumab + quimioterapia (ESMO)

Checkmate 9LA

First-line (1L) nivolumab (N) + ipilimumab (I) + chemotherapy (C) vs C alone in patients (pts) with metastatic NSCLC (mNSCLC) from **CheckMate 9LA**: 4-y clinical update and outcomes by tumor histologic subtype (THS)



Primary endpoint

- OS

Secondary endpoints

- PFS (BICR), ORR (BICR), safety

Exploratory endpoints

- OS by tumor histologic subtype

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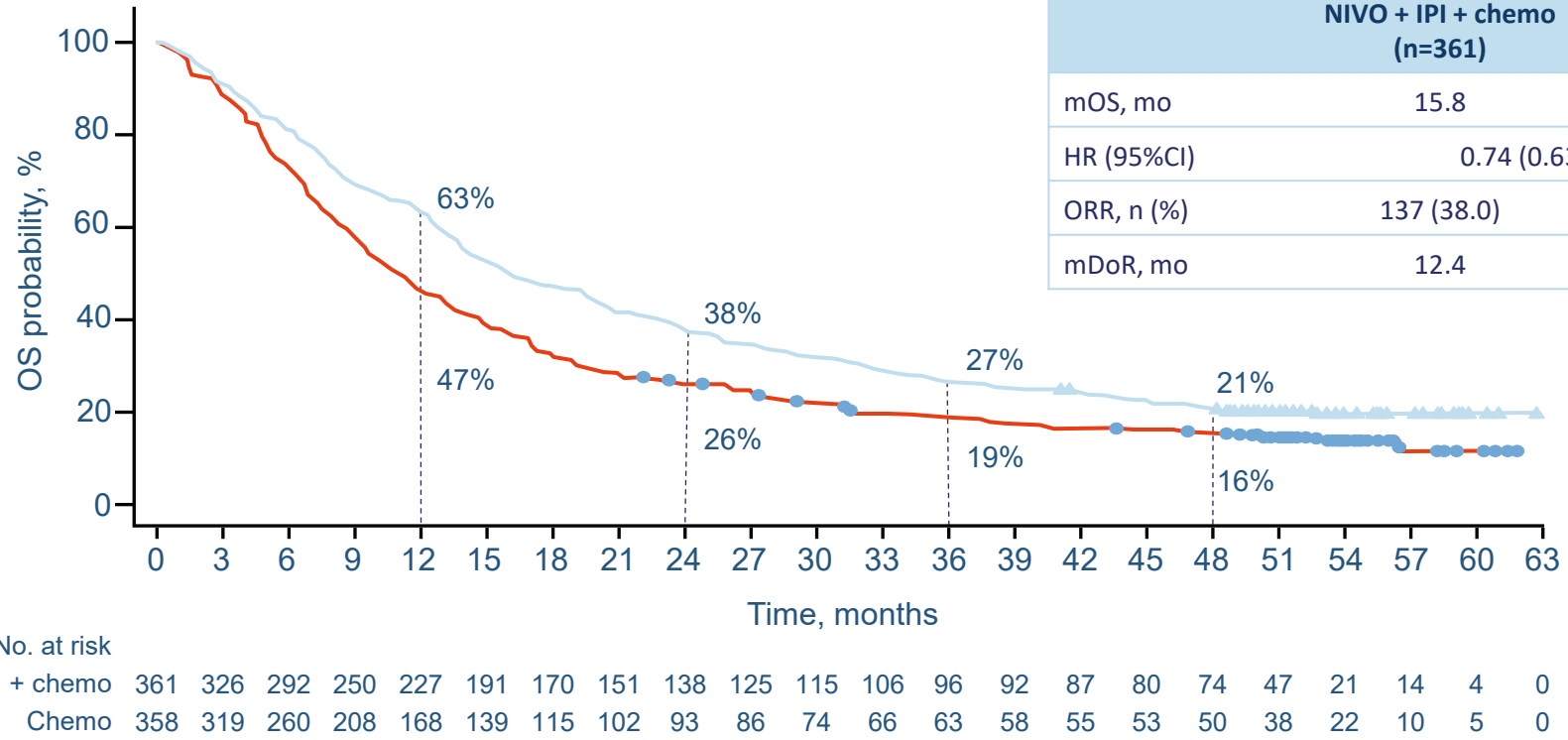
Carbone DP, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9023

Checkmate 9LA

4-year update: OS in all randomized patients



	NIVO + IPI + chemo (n=361)	Chemo (n=358)
mOS, mo	15.8	11.0
HR (95%CI)	0.74 (0.63, 0.87)	
ORR, n (%)	137 (38.0)	90 (25.1)
mDoR, mo	12.4	5.6

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Carbone DP, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9023

Checkmate 9LA

	NIVO + IPI + chemo	Chemo
PD-L1 <1%, n	135	129
mOS, mo	17.7	9.8
HR (95%CI)	0.66 (0.50, 0.86)	
ORR, n (%)	42 (31.1)	26 (20.2)
mDoR, mo	17.5	4.3
PD-L1 ≥1%, n	204	204
mOS, mo	15.8	10.9
HR (95%CI)	0.74 (0.60, 0.92)	
ORR, n (%)	87 (42.6)	56 (27.5)
mDoR, mo	11.8	5.6

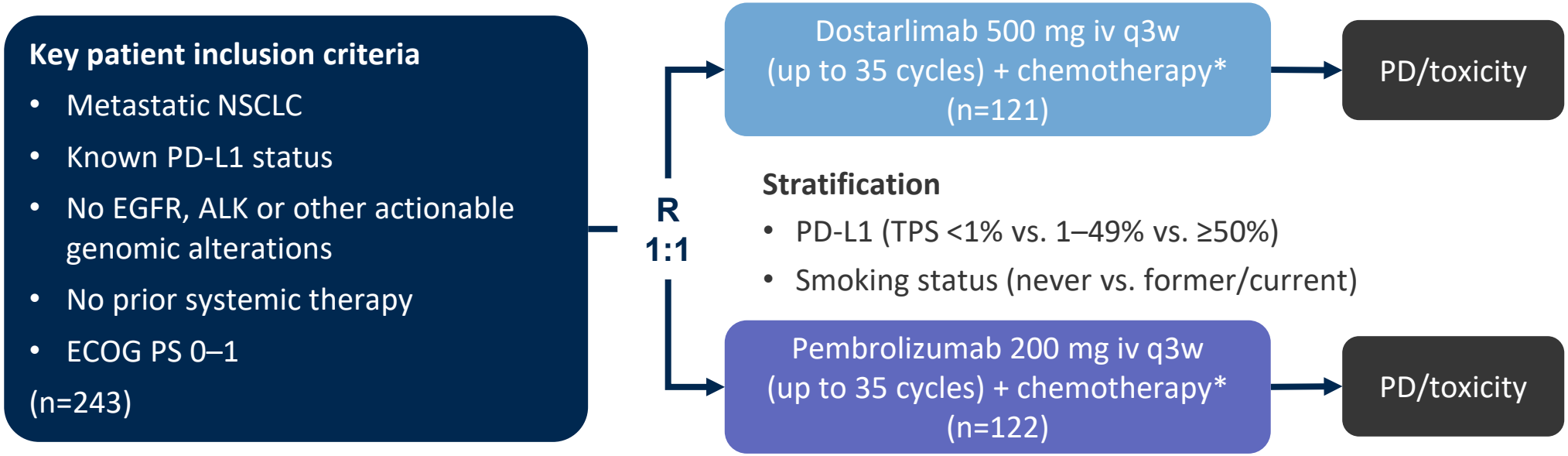
	NIVO + IPI + chemo	Chemo
Squamous, n	115	112
mOS, mo	14.5	9.1
HR (95%CI)	0.64 (0.48, 0.84)	
Nonsquamous, n	246	246
mOS, mo	17.8	12.0
HR (95%CI)	0.80 (0.66, 0.97)	
Solid tumors, n	80	87
mOS, mo	17.9	9.5
HR (95%CI)	0.70 (0.49, 0.99)	
Acinar tumors, n	63	53
mOS, mo	18.7	12.7
HR (95%CI)	0.77 (0.51, 1.15)	

Conclusiones: en pacientes con CPNCP Avanzado el esquema en 1aL nivolumab + ipilimumab + quimioterapia ofrece un beneficio en supervivencia sobre la quimioterapia sola, independientemente del estado de PD-L1 y el subtipo histológico

Carbone DP, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9023

PERLA

Overall survival from a phase II randomised double-blind trial (PERLA) of dostarlimab (dostar) + chemotherapy (CT) vs pembrolizumab (pembro) + CT in metastatic non-squamous NSCLC



Primary endpoint

- ORR (RECIST v1.1, BICR)

Secondary endpoints

- OS, PFS, safety

Peters S, et al. Ann Oncol 2023;34(suppl):Abstr LBA64

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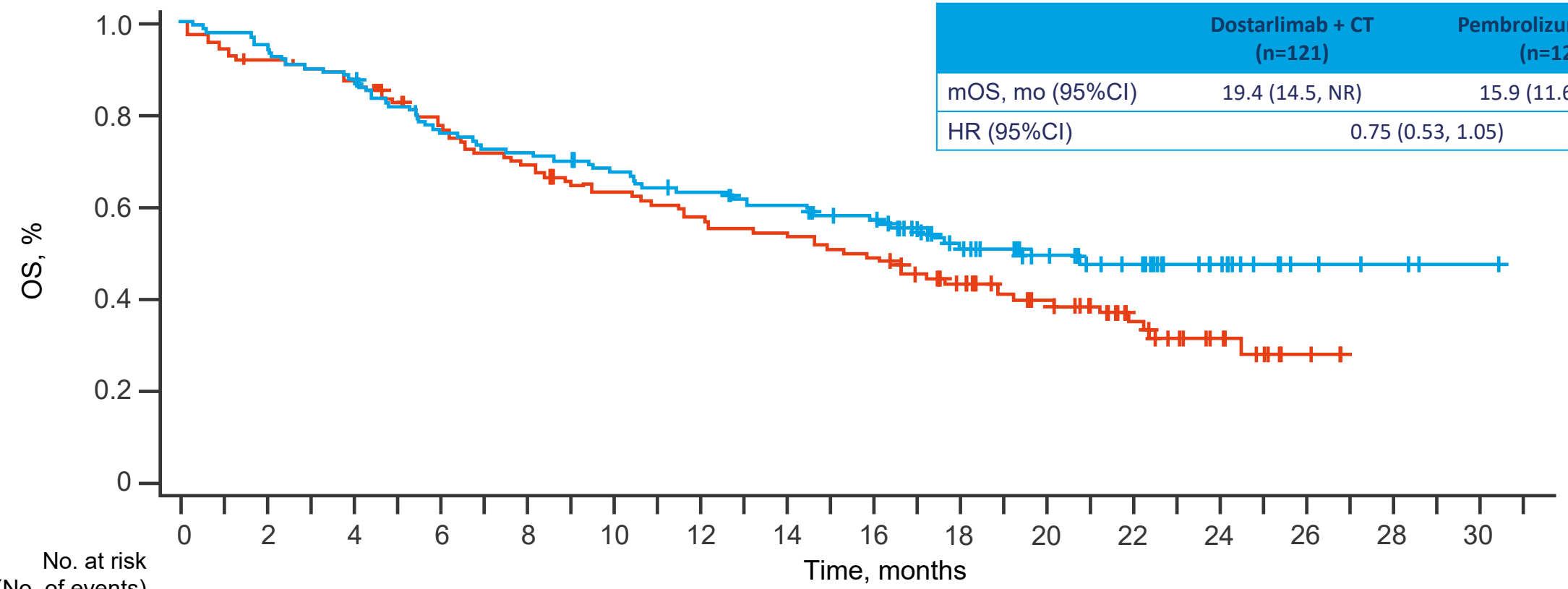
PERLA

Overall survival

	Dostarlimab + CT (n=121)	Pembrolizumab + CT (n=122)
mOS, mo (95%CI)	19.4 (14.5, NR)	15.9 (11.6, 19.3)
HR (95%CI)	0.75 (0.53, 1.05)	



No. at risk (No. of events)

Dostarlimab + CT	121	118	115	109	106	98	91	87	86	84	80	76	74	71	70	66	64	55	44	39	32	27	25	18	15	9	6	5	3	1	1	0
	(0)	(3)	(6)	(12)	(15)	(22)	(29)	(33)	(34)	(36)	(39)	(43)	(44)	(46)	(47)	(50)	(51)	(53)	(57)	(57)	(58)	(59)	(59)	(59)	(59)	(59)	(59)	(59)	(59)	(59)	(59)	(59)
Pembrolizumab + CT	122	115	111	109	105	99	92	84	81	76	73	70	67	64	62	59	57	47	42	34	31	26	20	15	11	6	3	0	0	0	0	0
	(0)	(7)	(10)	(12)	(16)	(21)	(27)	(34)	(37)	(41)	(44)	(47)	(50)	(53)	(55)	(58)	(60)	(64)	(66)	(68)	(69)	(69)	(72)	(74)	(74)	(75)	(75)	(75)	(75)	(75)	(74)	(75)

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Peters S, et al. Ann Oncol 2023;34(suppl):Abstr LBA64

Novedades para pacientes sin diana accionable

INMUNOTERAPIA

BONUS TRACK

WCLC

- STK11/LKB1 Deficient Phenotype Rather Than Mutation Diminishes Immunotherapy Efficacy in NSCLC: Results From Three Randomized Trials – Li A, et al → Estudio a partir de OAK, POPLAR y ORIENT-11. Peor supervivencia global en STK11 deficient, agravada si se añade sobreexpresión de RAS

- IMpower151: Phase III Study of Atezolizumab + Bevacizumab + Chemotherapy in 1L Metastatic Nonsquamous NSCLC – Zhou C, et al → Estudio negativo. Añadir atezolizumab a Bevacizumab + QT no aumenta la supervivencia (permitia EGFR/ALK)

ASCO

- CHOICE-01: A double-blind randomized phase 3 study of toripalimab versus placebo in combination chemotherapy for advanced NSCLC without EGFR/ALK mutations → Estudio positivo

Novedades para pacientes sin diana accionable

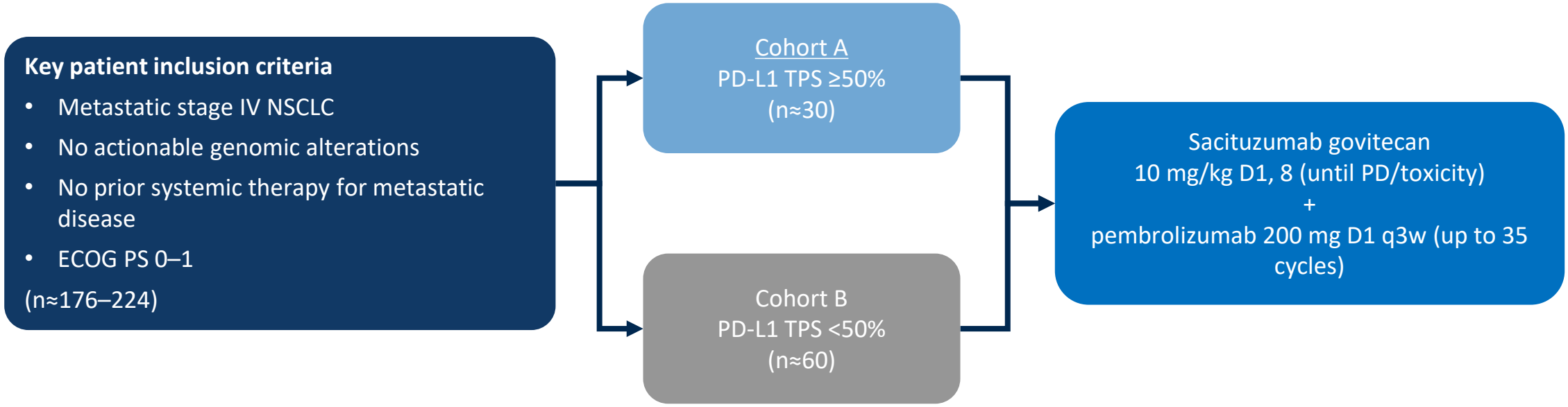
NO INMUNOTERAPIA

- EVOKE-02: **Sacituzumab Govitecan** + Pembrolizumab en 1aL (WCLC)

- TROPION-Lung01: **Datopotamab-deruxtecan** vs Docetaxel (ESMO)

EVOKE-02

Sacituzumab Govitecan + Pembrolizumab in 1L Metastatic Non-Small Cell Lung Cancer: Preliminary Results of the EVOKE-02 Study



Primary endpoints

- ORR, DLTs

Secondary endpoints

- DCR, DoR, PFS, OS, safety

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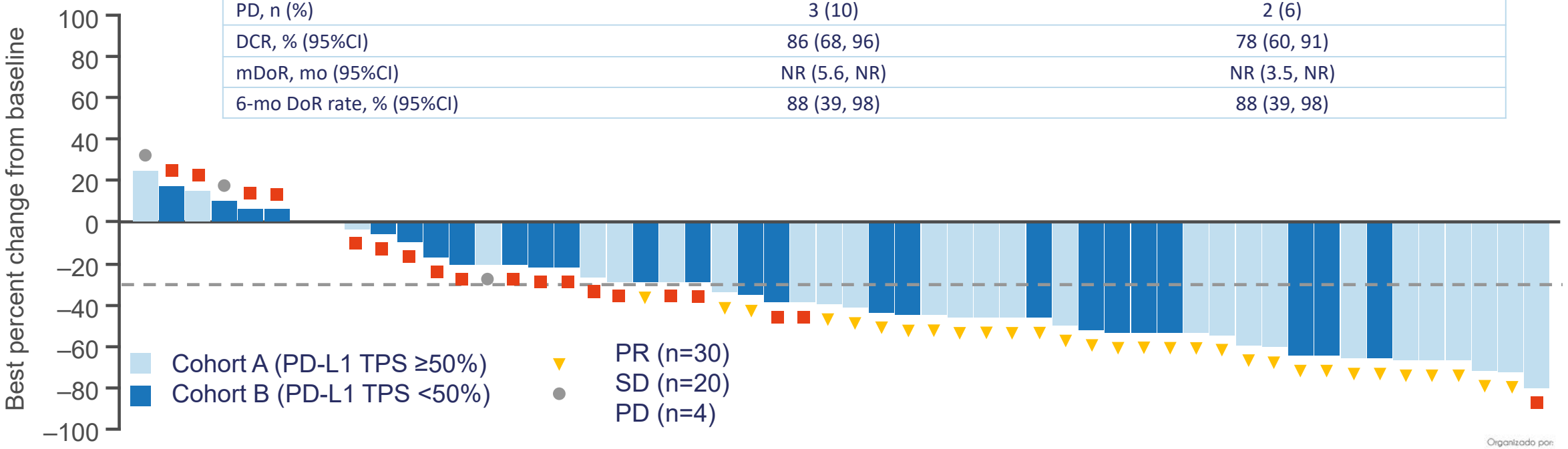
Cho BC, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA05.04

EVOKE-02

Efficacy	Cohort A (PD-L1 TPS ≥50%) Sacituzumab govitecan + pembrolizumab (n=29)	Cohort B (PD-L1 TPS <50%) Sacituzumab govitecan + pembrolizumab (n=32)
ORR, % (95%CI)	69 (49, 85)	44 (26, 62)
PR / cPR, n (%)	20 (69) / 18 (62)	14 (44) / 12 (38)
SD, n (%)	5 (17)	11 (34)
PD, n (%)	3 (10)	2 (6)
DCR, % (95%CI)	86 (68, 96)	78 (60, 91)
mDoR, mo (95%CI)	NR (5.6, NR)	NR (3.5, NR)
6-mo DoR rate, % (95%CI)	88 (39, 98)	88 (39, 98)



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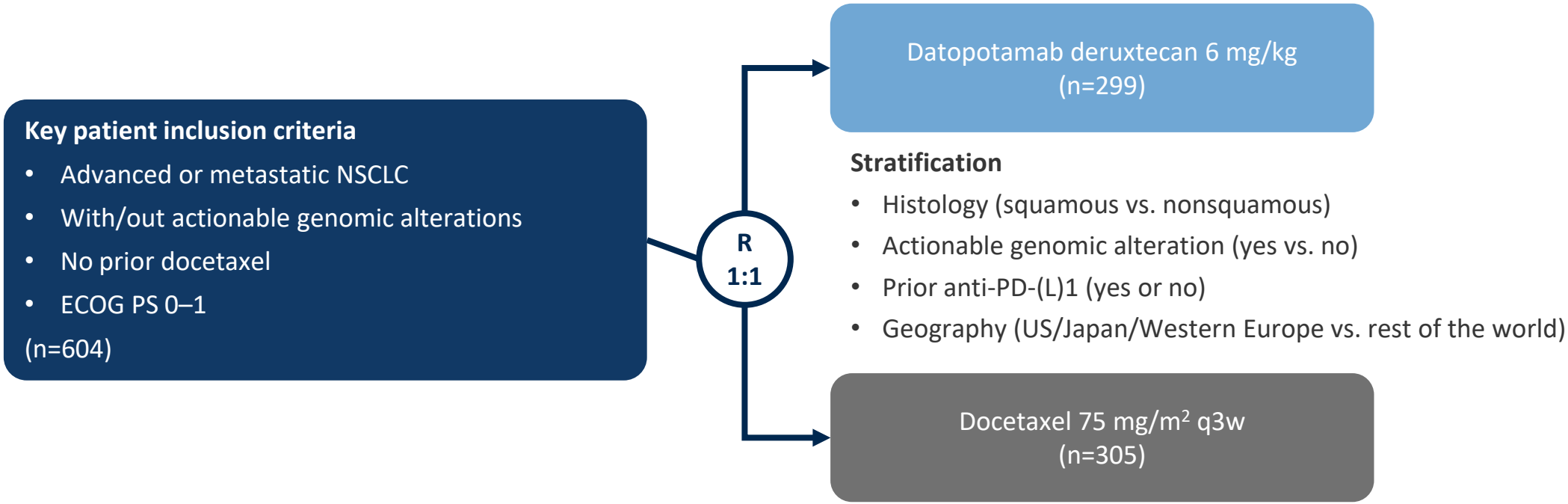
Cho BC, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA05.04

TROPION-Lung01

Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): results of the randomized phase 3 study TROPION-Lung01



Dual primary endpoints

- PFS (BICR), OS

Secondary endpoints

- ORR, DoR, safety

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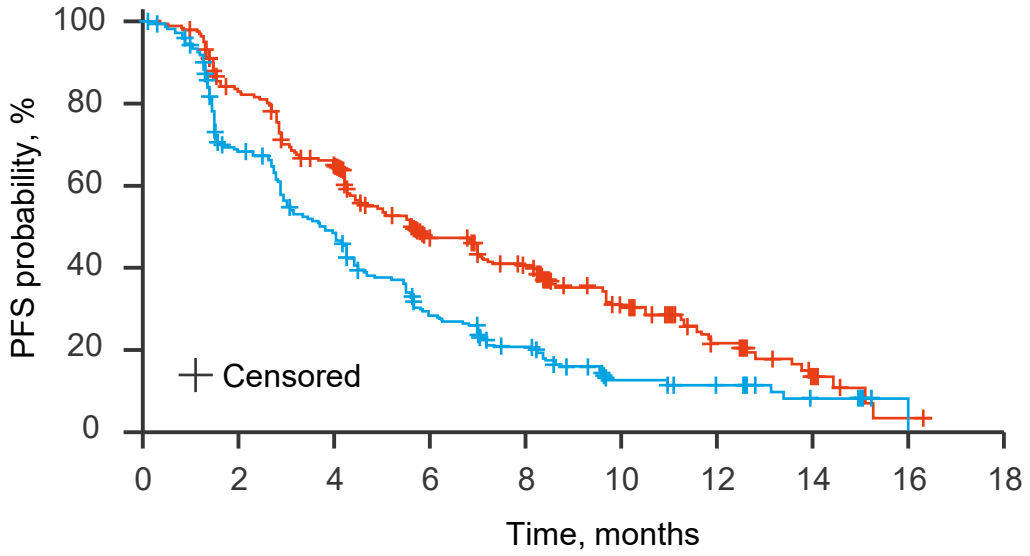
Lisberg AE, et al. Ann Oncol 2023;34(suppl):Abstr LBA12

TROPION-Lung01

PFS by histology (exploratory analysis)

Nonsquamous

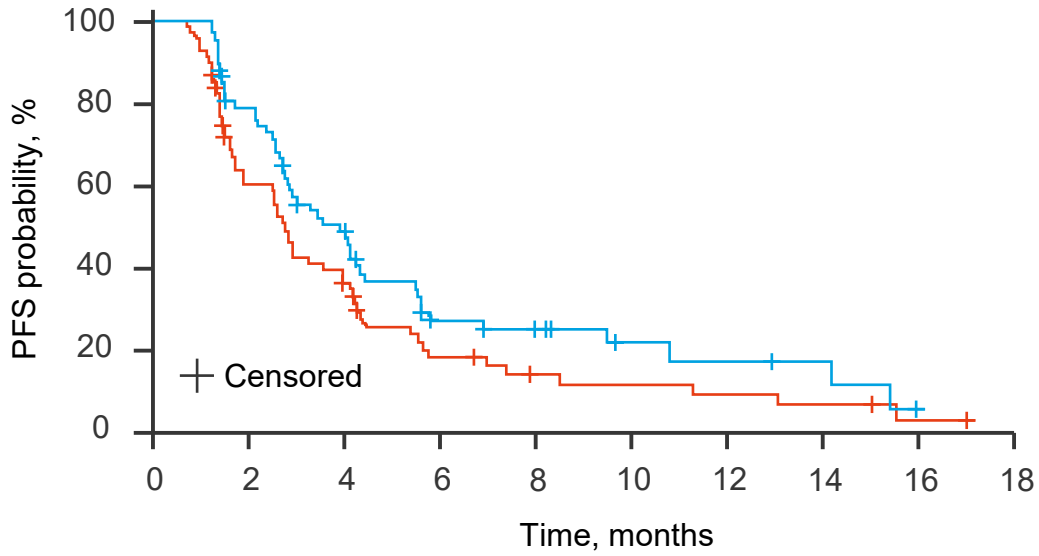


No. at risk

Dato-DXd	229	178	134	86	68	41	20	7	1	0
Docetaxel	232	135	90	50	32	14	10	4	0	0

	Dato-DXd	Docetaxel
mPFS, mo (95%CI)	5.6 (4.4, 7.0)	3.7 (2.9, 4.2)
HR (95%CI)	0.63 (0.51, 0.78)	
ORR, %	31.2	12.8
DoR, mo	7.7	5.6

Squamous



No. at risk

Dato-DXd	70	38	22	10	6	5	4	3	1	0
Docetaxel	73	51	30	13	10	5	4	3	0	0

	Dato-DXd	Docetaxel
mPFS, mo (95%CI)	2.8 (1.9, 4.0)	3.9 (2.8, 4.5)
HR (95%CI)	1.38 (0.94, 2.02)	
ORR, %	9.2	12.7
DoR, mo	5.9	8.1

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Lisberg AE, et al. Ann Oncol 2023;34(suppl):Abstr LBA12

Novedades para pacientes CON diana accionable

EGFR

- 1a línea de tratamiento:
  - FLAURA2: **Osimertinib + quimioterapia** vs Osimertinib (WCLC)
  - MARIPOSA: **Amivantanab + Lazertinib** vs Osimertinib (ESMO)
- 2a línea de tratamiento dirigido:
  - MARIPOSA2: **Amivantanab +/- Lazertinib** vs quimioterapia (ESMO)
- 2a línea: añadir inmunoterapia?
  - ATTLAS: **atezolizumab-bevacizumab**-quimioterapia (ESMO)
  - KEYNOTE-798: **quimioterapia-pembrolizumab** vs quimioterapia (ASCO)
  - ILLUMINATE: **durvalumab-tremelimumab**-quimioterapia (WCLC)

Novedades para pacientes CON diana accionable

EGFR ins20

- PAPILLON: **Amivantanab+quimioterapia** vs quimioterapia en 1a línea (ESMO)
- WU-QONG6: **Sunvozertinib** (ASCO)

MET exon 14

- **Savolitinib** en 1a línea(WCLC)

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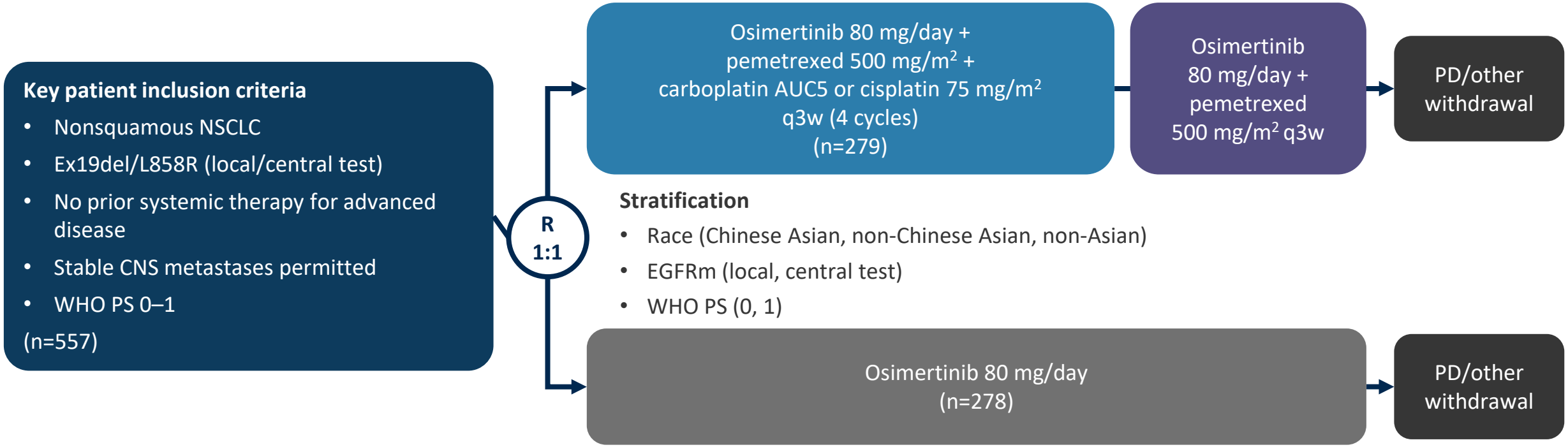
1aL: FLAURA2

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



Primary endpoint

- PFS (investigator-assessed, RECIST v1.1)

Secondary endpoints

- OS, ORR, DoR, DCR, PFS2, safety

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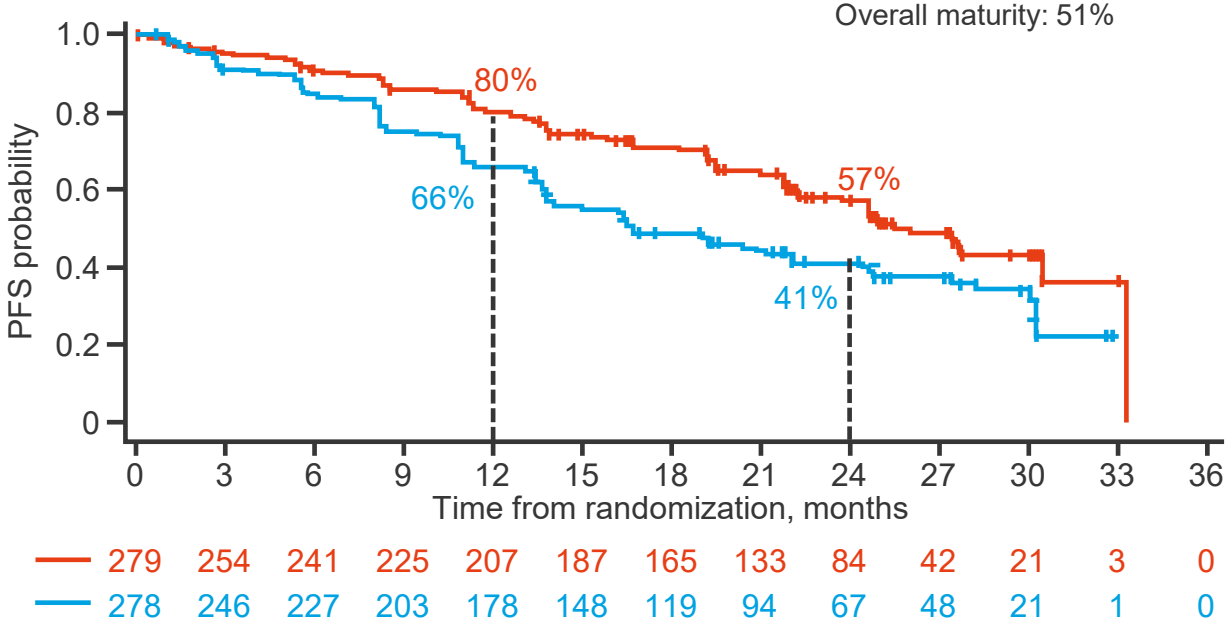
Janne P, et al. J Thorac Oncol 2023;18(suppl 9):Abstr PL03.13

1aL: FLAURA2

Progression-free survival

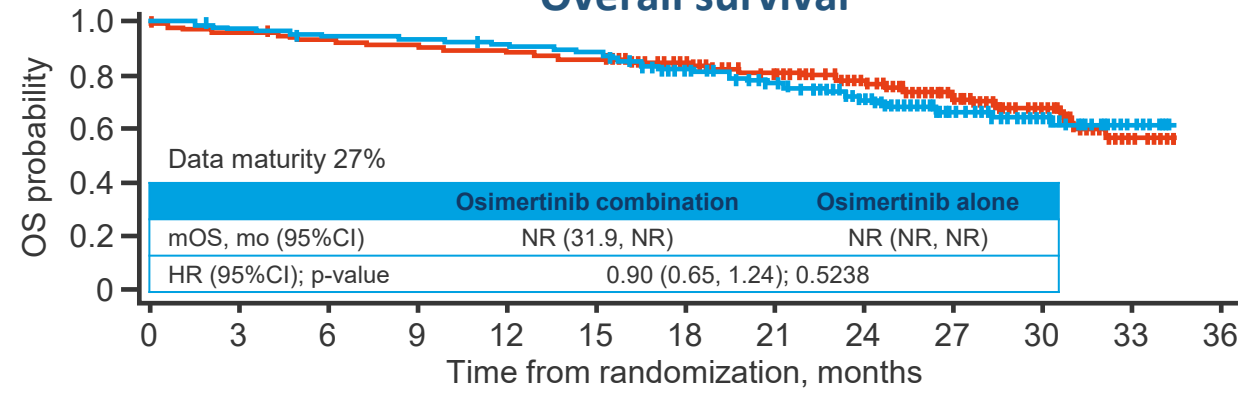
	Osimertinib combination	Osimertinib alone
mPFS, mo (95%CI)	25.5 (21.7, NR)	16.7 (14.1, 21.3)
Stratified HR (95%CI); p-value	0.62 (0.49, 0.79); <0.0001	
Median follow-up, mo (range)	19.5 (0–33.3)	16.5 (0–33.1)

Overall maturity: 51%



	Osimertinib combination	Osimertinib alone
With CNS metastases, n	116	110
mPFS, mo (95%CI)	24.9 (22.0, NR)	13.8 (11.0, 16.7)
HR (95%CI)	0.47 (0.33, 0.66)	
Without CNS metastases, n	163	168
mPFS, mo (95%CI)	27.6 (24.7, NR)	21.0 (16.7, 30.5)
HR (95%CI)	0.75 (0.55, 1.03)	

Overall survival



Data maturity 27%

	Osimertinib combination	Osimertinib alone
mOS, mo (95%CI)	NR (31.9, NR)	NR (NR, NR)
HR (95%CI); p-value	0.90 (0.65, 1.24); 0.5238	

Osimertinib combination — Osimertinib alone

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1aL: FLAURA2

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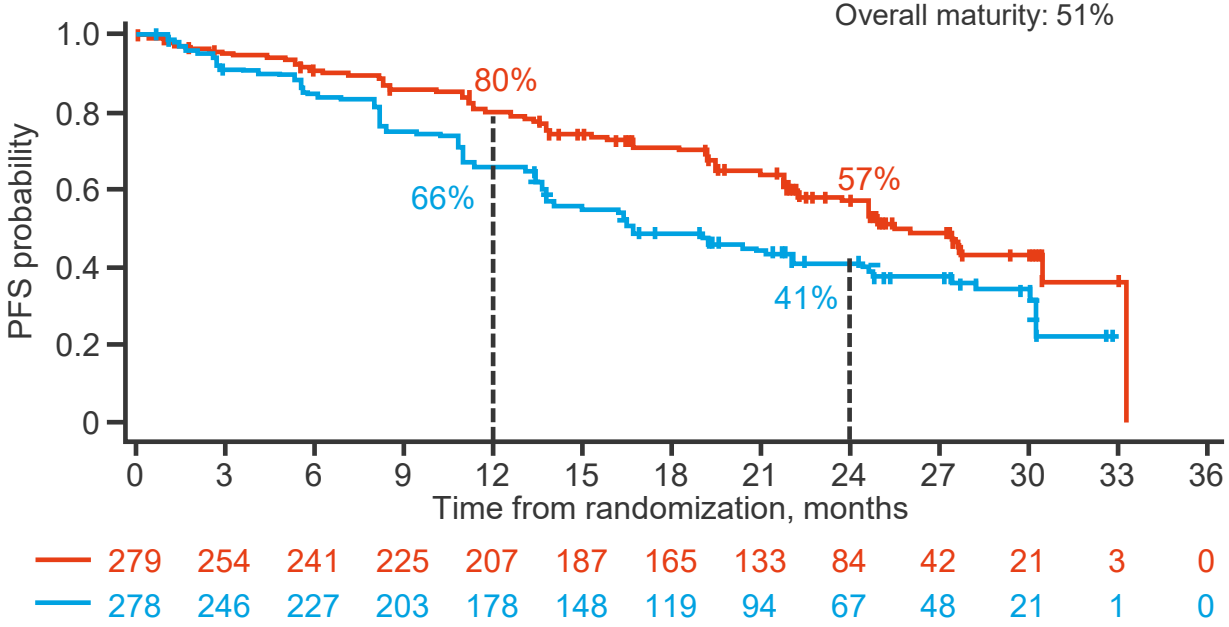

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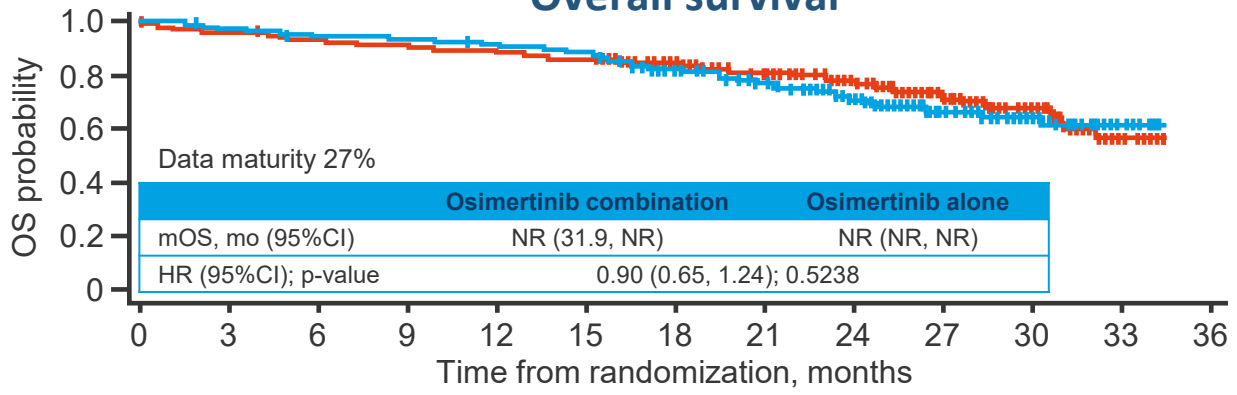
Overall survival



Data maturity 27%

	Osimertinib combination	Osimertinib alone
mOS, mo (95%CI)	NR (31.9, NR)	NR (NR, NR)
HR (95%CI); p-value	0.90 (0.65, 1.24); 0.5238	

Osimertinib combination — Osimertinib alone

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Janne P, et al. J Thorac Oncol 2023;18(suppl 9):Abstr PL03.13

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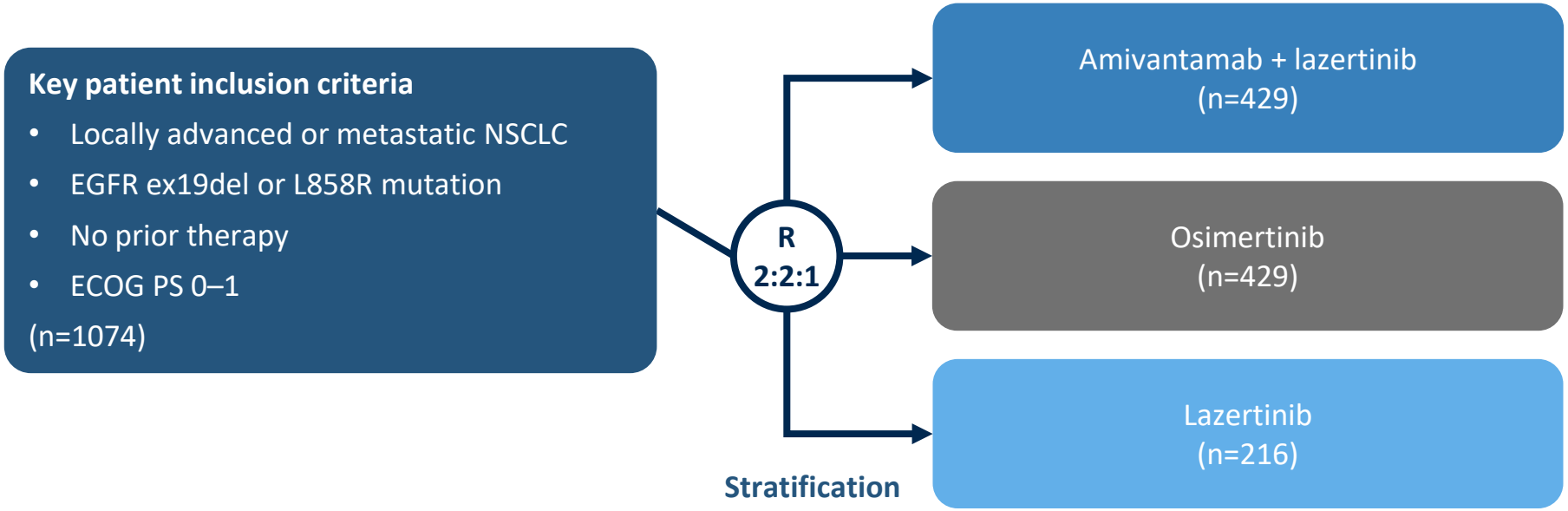
1aL MARIPOSA

Amivantamab plus lazertinib vs osimertinib as first-line treatment in patients with EGFR-mutated, advanced non-small cell lung cancer (NSCLC): Primary results from MARIPOSA, a phase 3, global, randomized, controlled trial



Primary endpoint

- PFS (RECIST v1.1, BICR)

Secondary endpoints

- OS, ORR, DoR, PFS2, safety

Cho BC, et al. Ann Oncol 2023;34(suppl):Abstr LBA14

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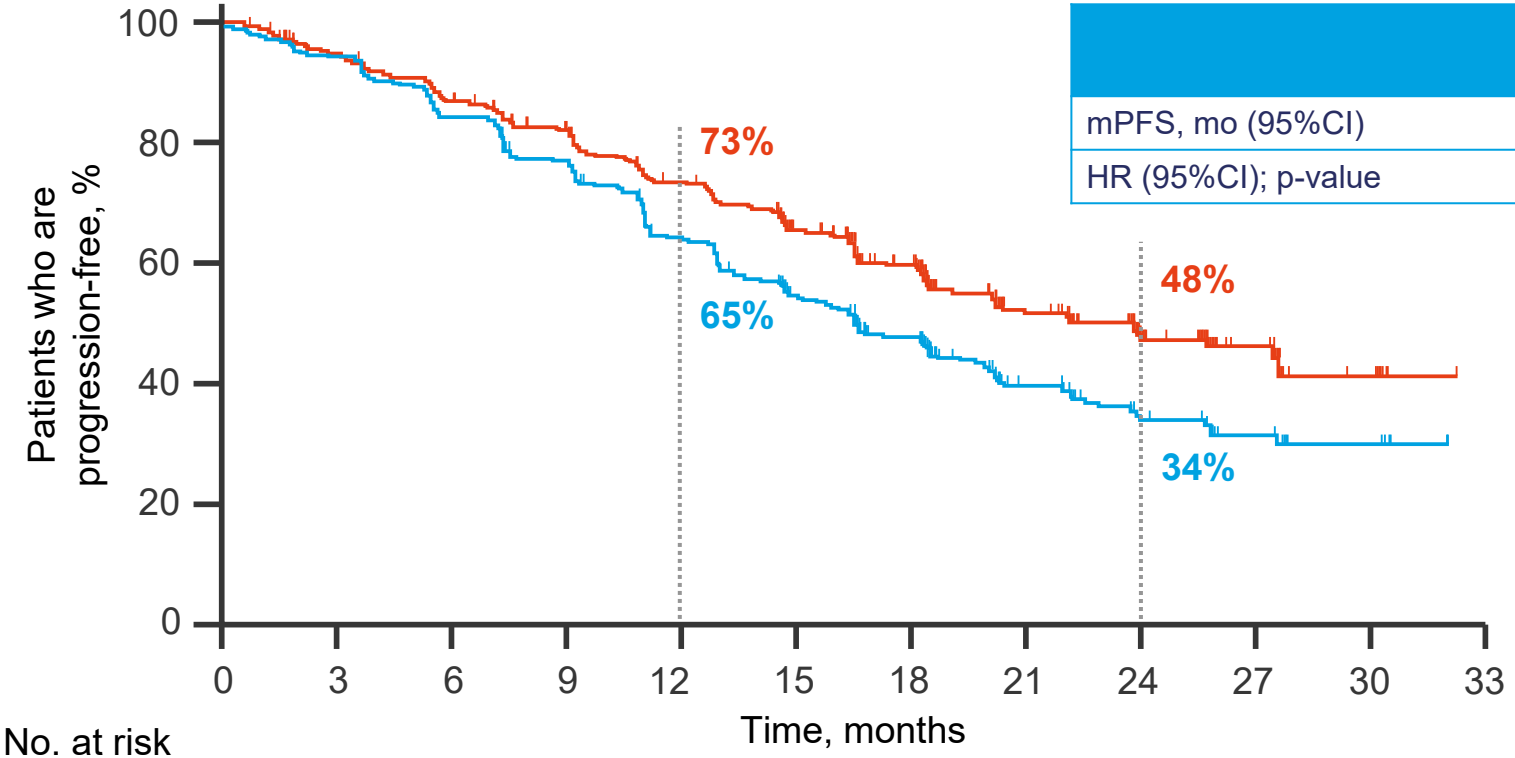
1aL MARIPOSA

Progression-free survival



	Amivantamab + lazertinib	Osimertinib
mPFS, mo (95%CI)	23.7 (19.1, 27.7)	16.6 (14.8, 18.5)
HR (95%CI); p-value	0.70 (0.58, 0.85); <0.001	

No. at risk

Amivantamab + lazertinib	429	391	357	332	291	244	194	106	60	33	8	0
Osimertinib	429	404	358	325	266	205	160	90	48	28	10	0

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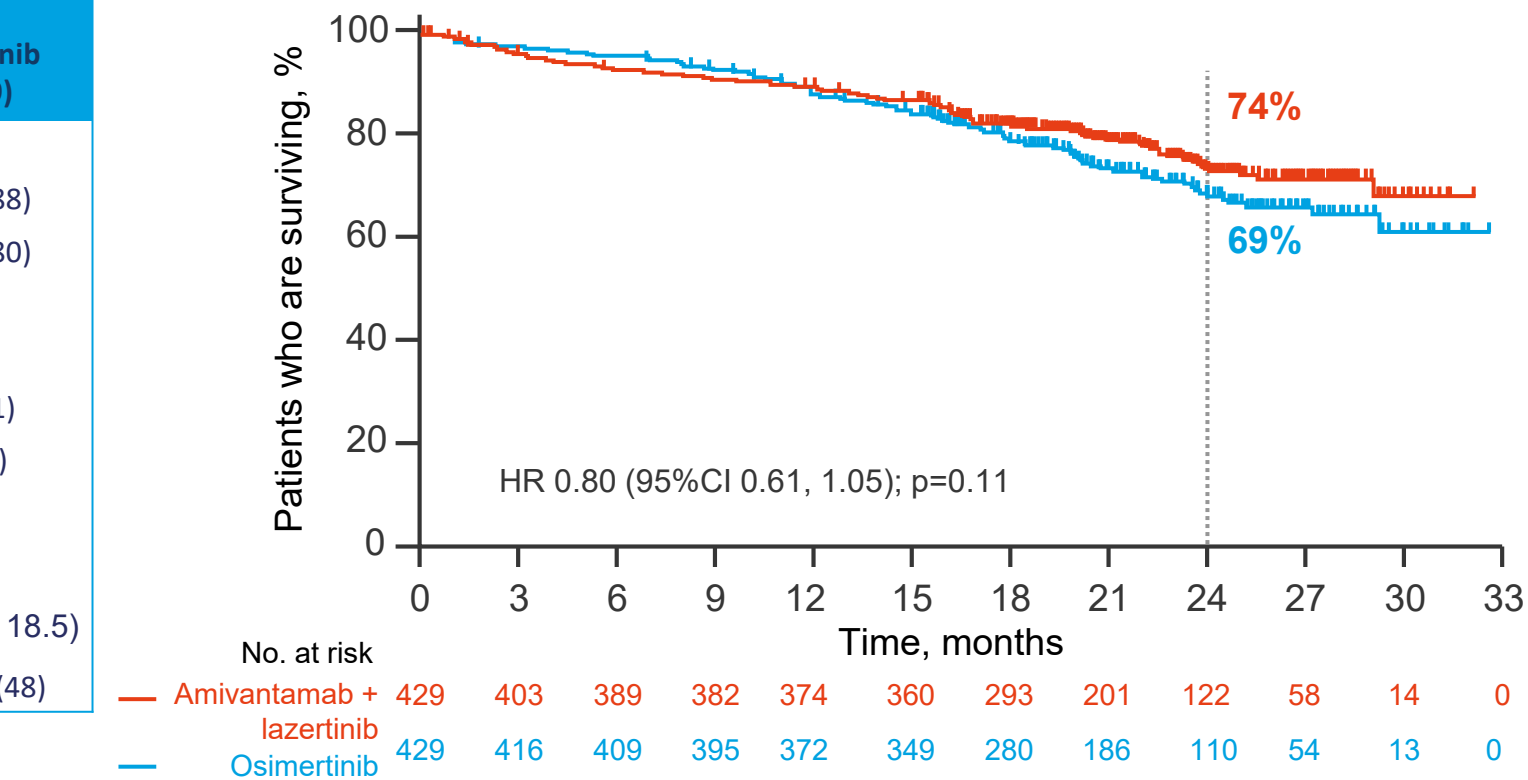
Cho BC, et al. Ann Oncol 2023;34(suppl):Abstr LBA14

1aL MARIPOSA

BICR-assessed response, n (%)	Amivantamab + lazertinib (n=429)	Osimertinib (n=429)
ORR, % (95%CI)		
All responders	86 (83, 89)	85 (81, 88)
Confirmed responders	80 (76, 84)	76 (71, 80)
BOR, n (%)		
CR	29 (7)	15 (4)
PR	334 (79)	335 (81)
SD	30 (7)	42 (10)
PD	7 (2)	11 (3)
NE/unknown	21 (5)	11 (3)
mDoR, mo (95%CI)[a]	25.8 (20.1, NE)	16.8 (14.8, 18.5)
Ongoing responses, n/N (%)	209/336 (62)	151/314 (48)

Interim overall survival



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Cho BC, et al. Ann Oncol 2023;34(suppl):Abstr LBA14

Safety

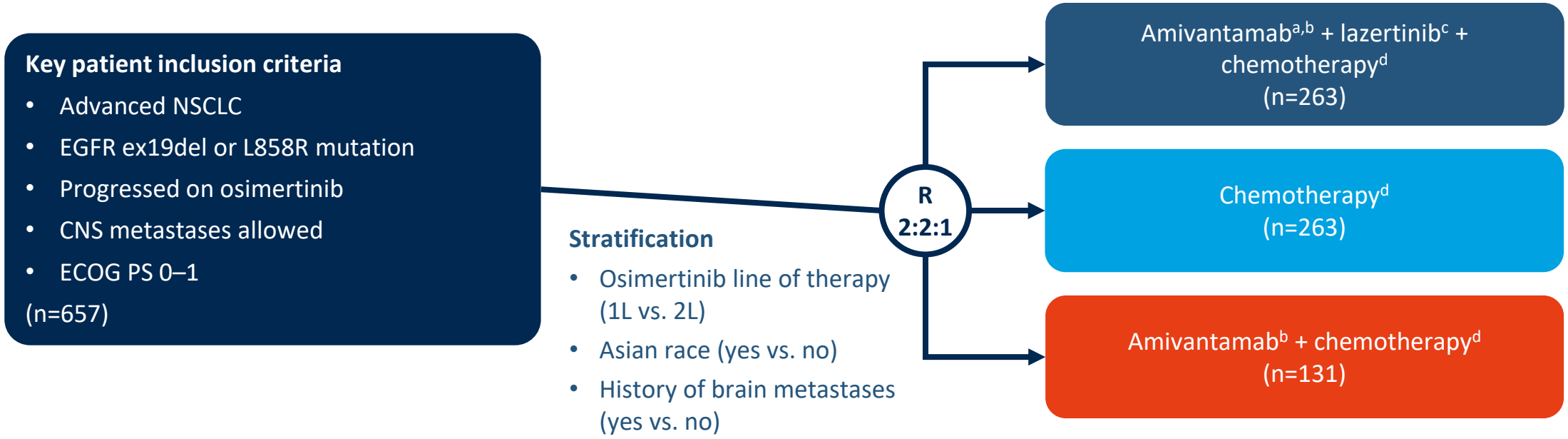
TEAE, n (%)	Amivantamab + lazertinib (n=421)	Osimertinib (n=428)
Any	421 (100)	425 (99)
Grade ≥3	316 (75)	183 (43)
Serious	205 (49)	143 (33)
Led to death	34 (8)	31 (7)
Led to treatment		
Interruptions of any agent	350 (83)	165 (39)
Reductions of any agent	249 (59)	23 (5)
Discontinuations of any agent	147 (35)	58 (14)

AEs, %	Amivantamab + lazertinib (n=421)		Osimertinib (n=428)	
	Grade 1–2	Grade ≥3	Grade 1–2	Grade ≥3
Related to EGFR inhibition	57	11	28	0.5
Paronychia	46	15	30	1
Rash	27	2	44	1
Diarrhea	21	8	13	0
Stomatitis	28	1	21	0.2
Pruritus	23	0.5	17	0.2
Related to MET inhibition				
Hypoalbuminemia	43	5	6	0
Peripheral edema	34	2	6	0

Cho BC, et al. Ann Oncol 2023;34(suppl):Abstr LBA14

2aL MARIPOSA-2

Amivantamab plus chemotherapy (with or without lazertinib) vs chemotherapy in EGFR-mutated advanced NSCLC after progression on osimertinib: MARIPOSA-2, a phase 3, global, randomized, controlled trial



Primary endpoint

- PFS (RECIST v1.1, BICR)

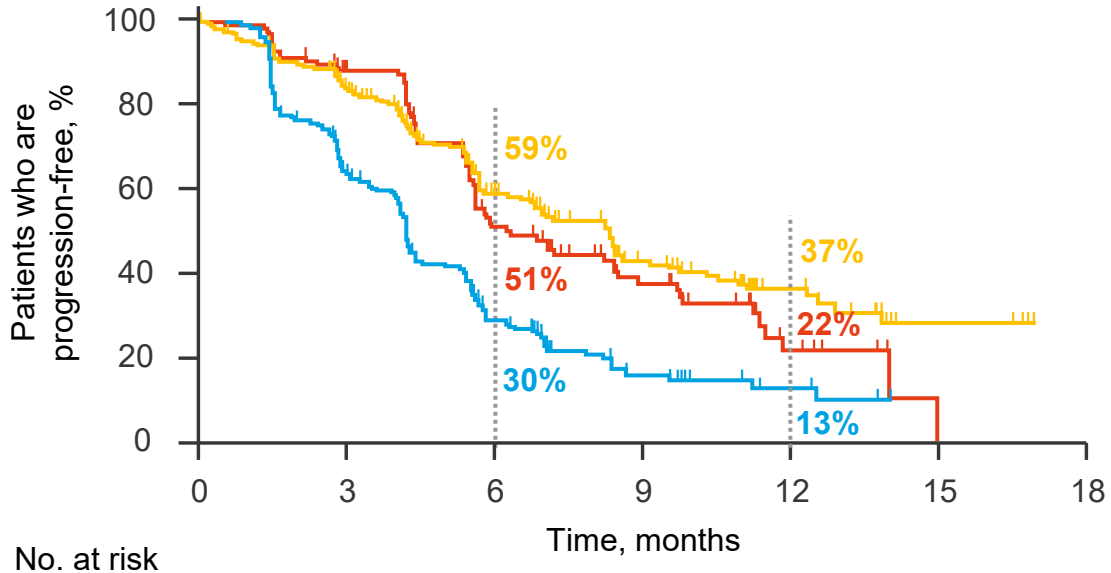
Secondary endpoints

- ORR, DoR, OS, intracranial PFS, PFS2, safety

Passaro A, et al. Ann Oncol 2023;34(suppl):Abstr LBA15

2aL MARIPOSA-2

PFS (BICR)

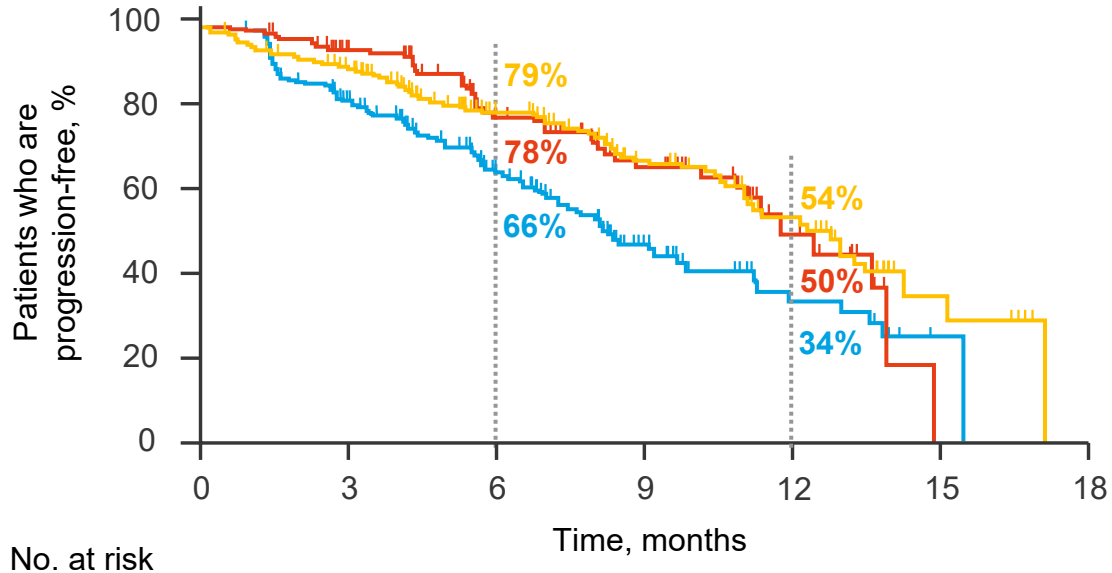


No. at risk

Amivantamab-chemotherapy	131	99	49	27	7	0	0
Amivantamab-lazertinib-chemotherapy	263	194	104	52	21	4	0
Chemotherapy	263	135	49	17	6	0	0

	Amivantamab + chemo vs. Chemo	Amivantamab + lazertinib + chemo[a] vs. Chemo
mPFS, mo	6.3 vs. 4.2	8.3 vs. 4.2
HR (95%CI); p-value[b]	0.48 (0.36, 0.64); <0.001	0.44 (0.35, 0.56); <0.001

Intracranial PFS (BICR)



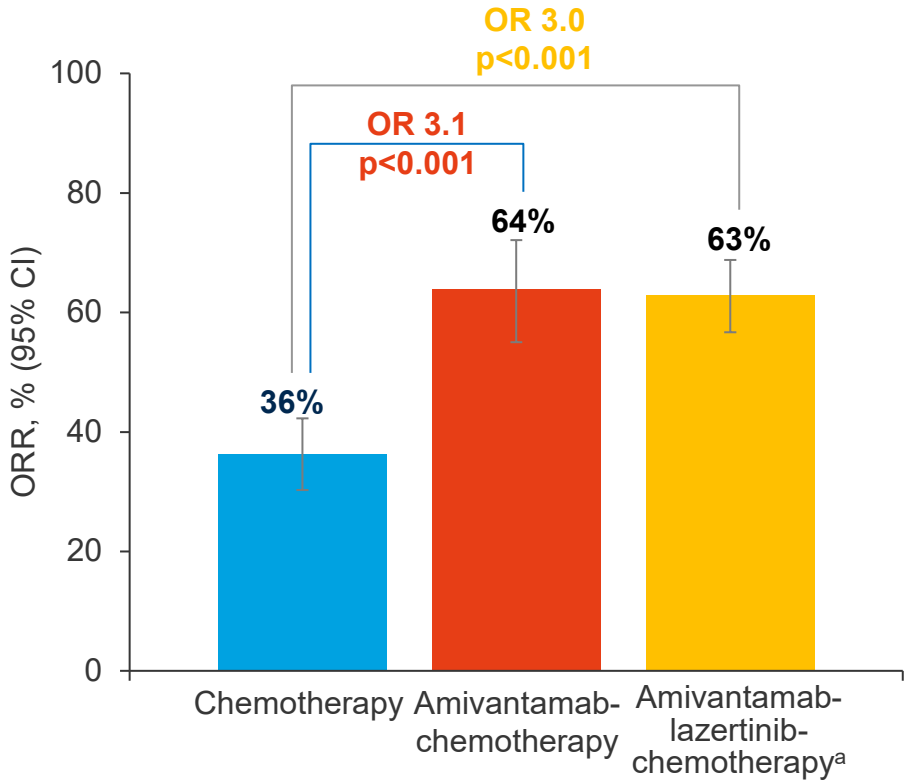
No. at risk

Amivantamab-chemotherapy	131	103	72	40	11	0	0
Amivantamab-lazertinib-chemotherapy	263	211	135	74	32	6	0
Chemotherapy	263	167	89	37	13	1	0

	Amivantamab + chemo vs. Chemo	Amivantamab + lazertinib + chemo[a] vs. Chemo
Median icPFS, mo	12.5 vs. 8.3	12.8 vs. 8.3
HR (95%CI); p-value[b]	0.55 (0.38, 0.79); 0.001	0.58 (0.44, 0.78); <0.001

Passaro A, et al. Ann Oncol 2023;34(suppl):Abstr LBA15

2aL MARIPOSA-2



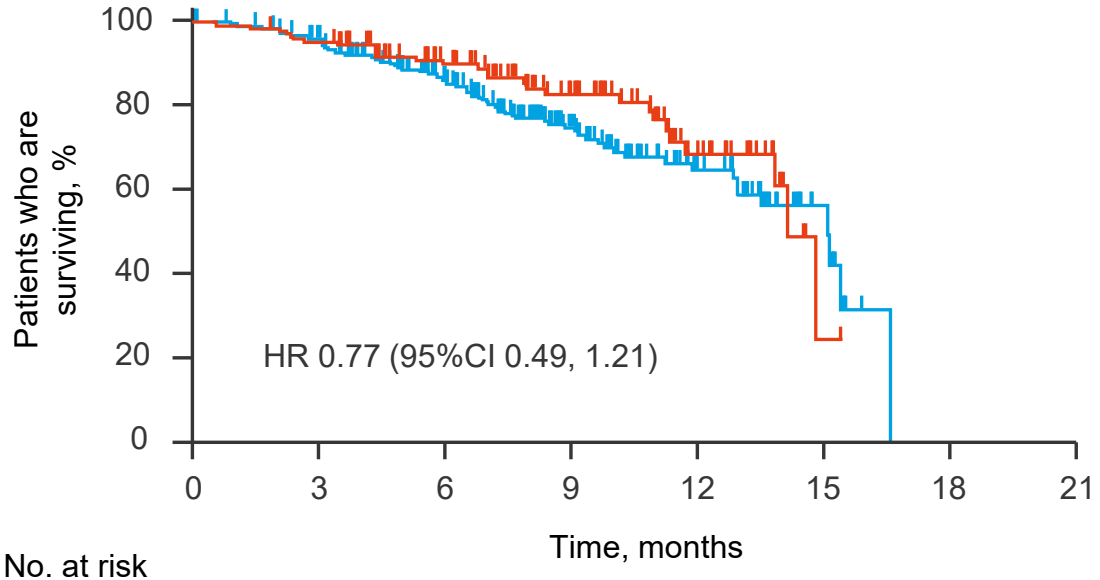
ORR and DoR (BICR)

BICR-assessed response[b]	Chemotherapy (n=263)	Amivantamab-chemotherapy (n=131)	Amivantamab + lazertinib + chemotherapy (n=263)
BOR, n (%)			
CR	1 (0.4)	2 (2)	6 (2)
PR	93 (36)	81 (62)	157 (61)
SD	82 (32)	30 (23)	61 (24)
PD	52 (20)	10 (8)	14 (5)
NE/unknown	32 (12)	7 (5)	21 (8)
mDoR, mo (95%CI)[b]	5.6 (4.2, 9.6)	6.9 (5.5, NE)	9.4 (6.9, NE)

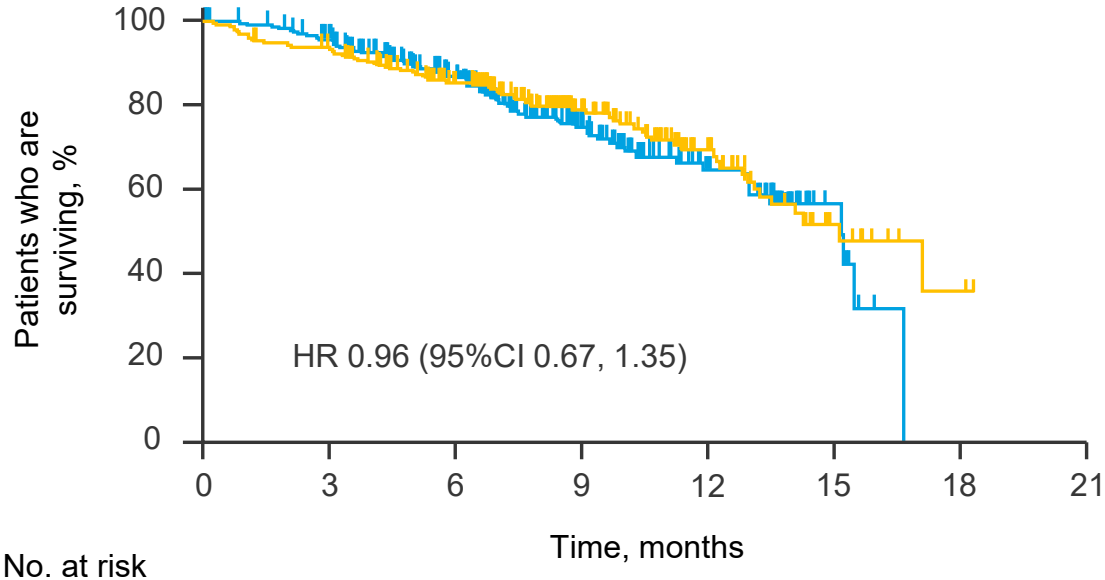
Passaro A, et al. Ann Oncol 2023;34(suppl):Abstr LBA15

2aL MARIPOSA-2

Early interim overall survival



No. at risk							
Amivantamab + chemotherapy	131	122	89	54	24	1	0
Chemotherapy	263	229	158	85	39	8	0



No. at risk								
Amivantamab-lazertinib -chemotherapy	263	241	170	101	52	13	3	0
Chemotherapy	263	229	158	85	39	8	0	0

Organizado por:
GECP lung cancer research

ESMO Congress 2023

Passaro A, et al. Ann Oncol 2023;34(suppl):Abstr LBA15

2aL: Añadir inmunoterapia?

ATTLAS: **atezolizumab-bevacizumab**-taxano-platino vs platino-pemetrexed (ESMO)

⇓

Positivo para EPP: Mejoría en PFS

No diferencias en OS

Organizado por: GECP lung cancer research

Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000 / Ahn M-J, et al. Ann Oncol 2023;34(suppl):Abstr LBA67 / Lee C, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA09.04

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⇓

Positivo para EPP: Mejoría en PFS

No diferencias en OS

KEYNOTE-798: **platino-pemetrexed-pembrolizumab** vs platino-pemetrexed (ASCO)

⇓

Negativo: no diferencias en PFS ni OS

Organizado por: GECP lung cancer research

Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000 / Ahn M-J, et al. Ann Oncol 2023;34(suppl):Abstr LBA67 / Lee C, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA09.04

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ATTLAS: **atezolizumab-bevacizumab**-taxano-platino vs platino-pemetrexed (ESMO)

⇓

Positivo para EPP: Mejoría en PFS

No diferencias en OS

KEYNOTE-798: **platino-pemetrexed-pembrolizumab** vs platino-pemetrexed (ASCO)

⇓

Negativo: no diferencias en PFS ni OS

ILLUMINATE: **durvalumab-tremelimumab**-platino-pemetrexed (WCLC)

⇓

Efecto antitumoral mas efectivo en pacientes con T790M- y PD-L1 >50%

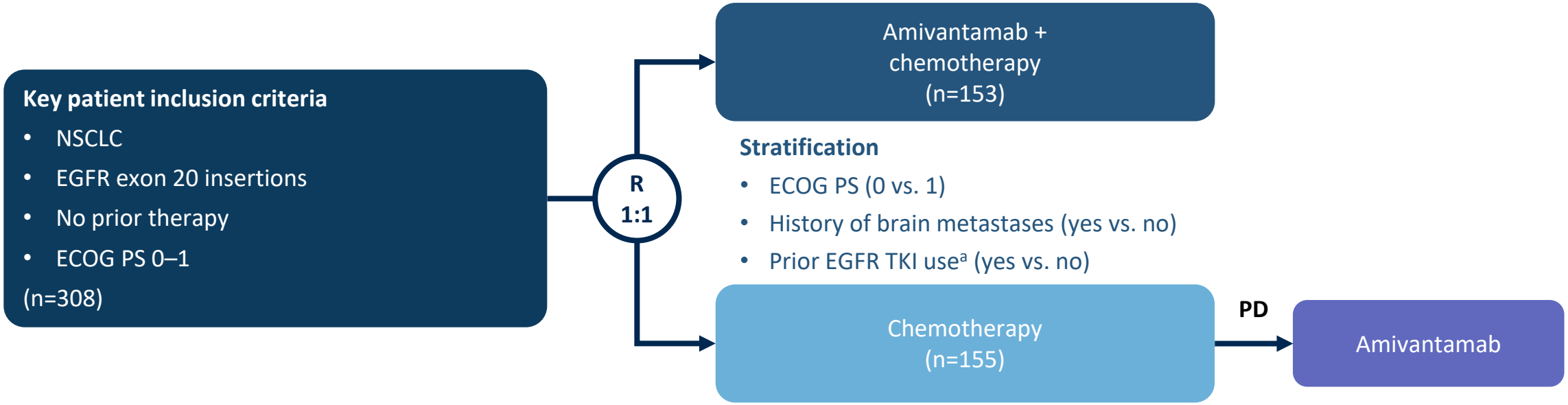
No comparado con SoC

Organizado por: GECP lung cancer research

Yang JC, et al. J Clin Oncol 2023;41(suppl 16):Abstr LBA9000 / Ahn M-J, et al. Ann Oncol 2023;34(suppl):Abstr LBA67 / Lee C, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA09.04

Ins20: PAPILLON

Amivantamab plus chemotherapy vs chemotherapy as first-line treatment in EGFR exon 20 insertion-mutated advanced non-small cell lung cancer (NSCLC): Primary results from PAPILLON, a randomized phase 3 global study



Primary endpoint

- PFS (RECIST v1.1, BICR)

Secondary endpoints

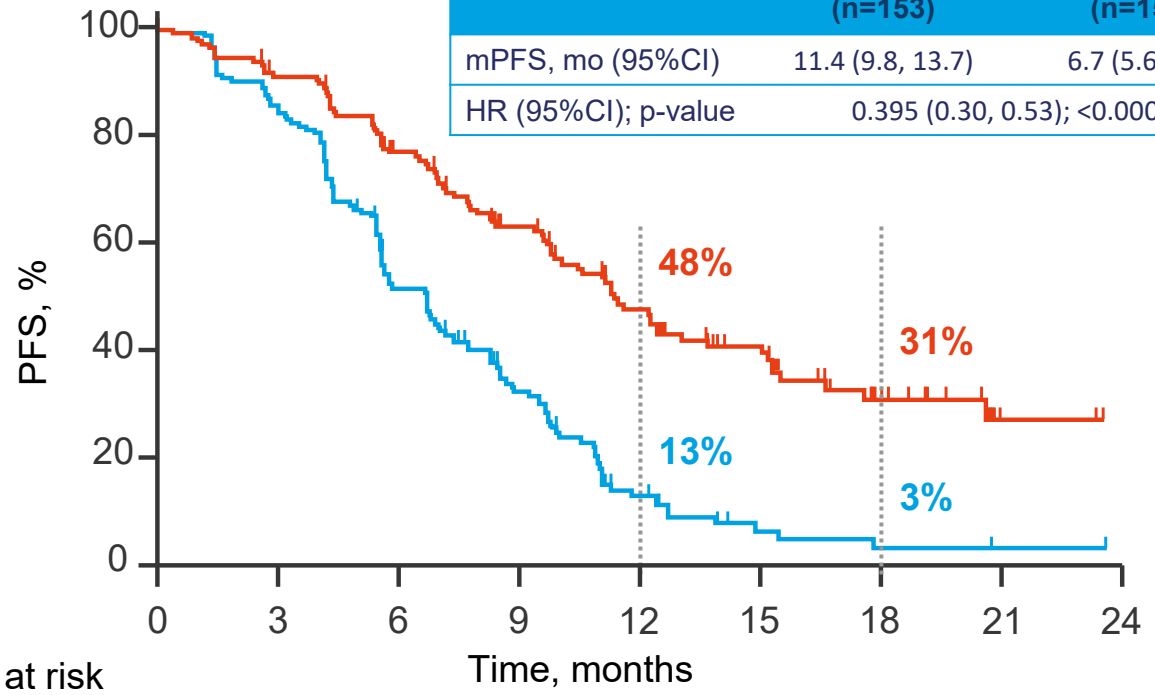
- ORR, DoR, OS, PFS2, safety

Girard N, et al. Ann Oncol 2023;34(suppl):Abstr LBA5

Ins20: PAPILLON

Progression-free survival (BICR)

	Amivantamab + chemotherapy (n=153)	Chemotherapy (n=155)
mPFS, mo (95%CI)	11.4 (9.8, 13.7)	6.7 (5.6, 7.3)
HR (95%CI); p-value	0.395 (0.30, 0.53); <0.0001	



No. at risk

Amivantamab + chemotherapy	153	135	105	74	50	33	15	3	0
Chemotherapy	155	131	74	41	14	4	2	1	0

BICR-assessed response[b]	Amivantamab + chemotherapy (n=153)	Chemotherapy (n=155)
Mean percent change of SoD, %	−53	−34
ORR, % (95%CI)	73 (65, 80)	47 (39, 56)
OR (95%CI); p-value	3.0 (1.8, 4.8); <0.0001	
BOR, n (%)		
CR	6 (4)	1 (1)
PR	105 (69)	71 (47)
SD	29 (19)	62 (41)
PD	4 (3)	16 (11)
NE/Unknown	8 (5)	2 (1)
Median time to response, weeks (range)	6.7 (5.1–72.5)	11.4 (5.1–60.2)

Organizado por: GECP lung cancer research

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Girard N, et al. Ann Oncol 2023;34(suppl):Abstr LBA5

Ins20: WU-QONG6

Sunvozertinib for the treatment of NSCLC with EGFR Exon20 insertion mutations: The first pivotal study results

Key patient inclusion criteria

- Locally advanced or metastatic NSCLC
- EGFR exon20 insertion mutation (local or central)
- 1–3 prior lines of systemic therapy
- PD on or after platinum-based chemotherapy

(n=104)

→ Sunvozertinib 300 mg/day

Primary endpoint

- ORR (IRC)

Secondary endpoints

- DoR, PFS, DCR, OS, safety

Wang M, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9002

Ins20: WU-QONG6

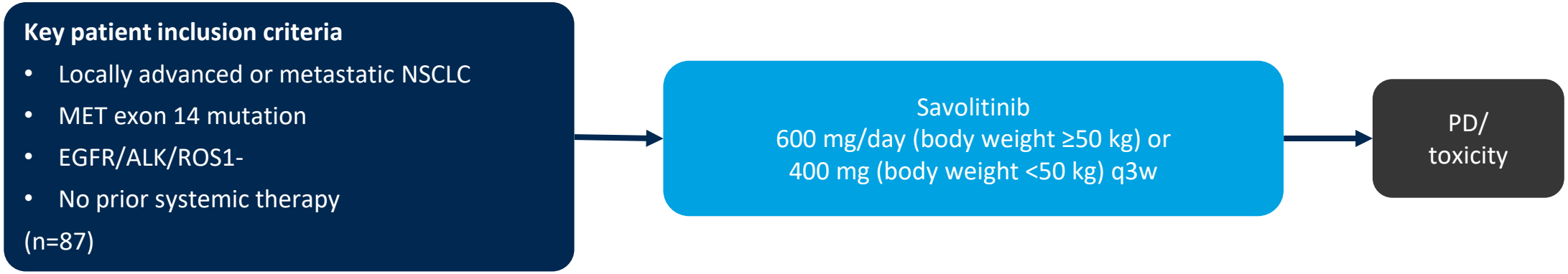
Response	Sunvozertinib (n=97)
ORR, n (%) [95%CI]; p-value	59 (60.8) [50.4, 70.6]; <0.0001
BOR, n (%)	
PR (confirmed)	59 (60.8)
SD	26 (26.8)
PD	6 (6.2)
NR	6 (6.2)
DCR, n (%) [95%CI]	85 (87.6) [79.4, 93.4]

EGFR Ex20ins subtypes	Sunvozertinib (n=97)
C-helical, n	2
ORR, %	100
DCR, %	100
Near loop, n	71
ORR, %	62.0
DCR, %	88.7
Far loop, n	24
ORR, %	54.2
DCR, %	83.3

Wang M, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9002

MET exon14: SAVOLITINIB

A Phase 3b Study of 1L Savolitinib in Patients with Locally Advanced or Metastatic NSCLC Harboring MET Exon 14 Mutation



Primary endpoint

- ORR (ICR, RECIST v1.1)

Secondary endpoints

- DCR, DoR, TTR, PFS, OS, safety

Organizado por: GECP lung cancer research

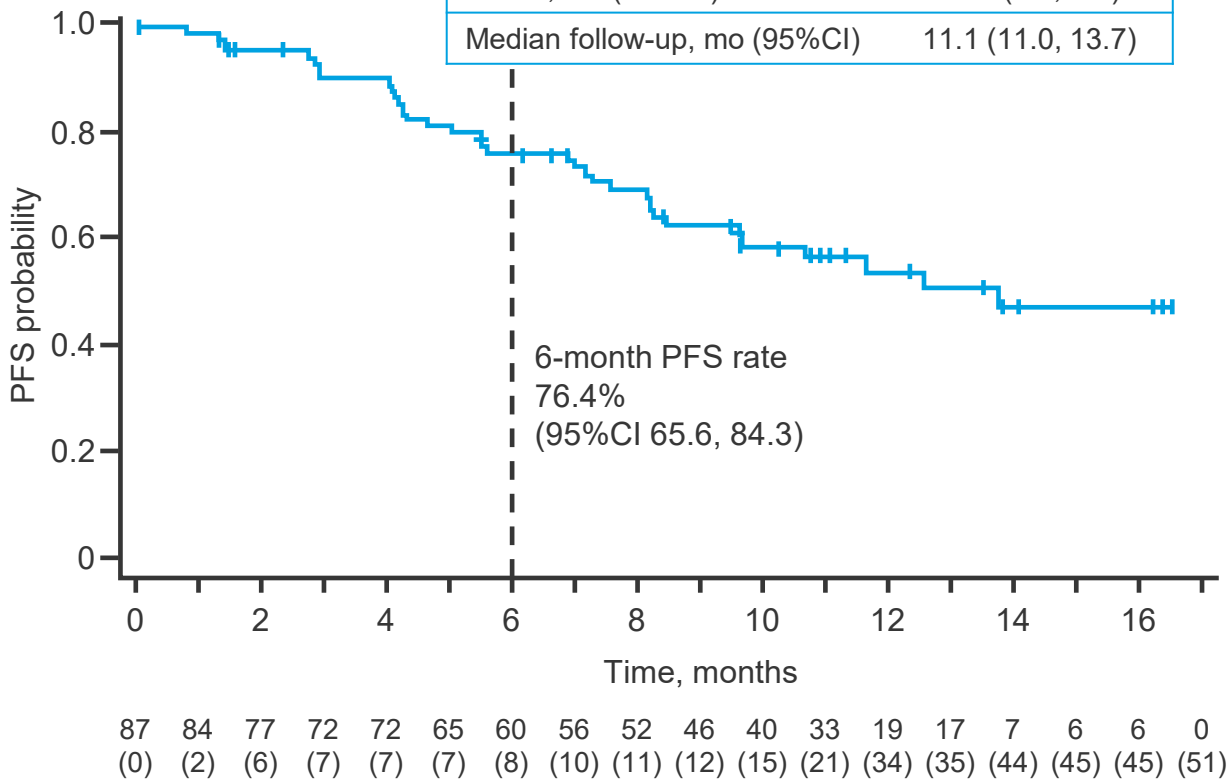
Lu S, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA21.03

MET exon14: SAVOLITINIB

	n=87
ORR, n (%) [95%CI]	51 (58.6)
BOR, n (%)	
PR	51 (58.6)
SD	29 (33.3)
PD	5 (5.7)
NE	2 (2.3)
DCR, n (%) [95%CI]	80 (92.0) [84.1, 96.7]
DoR, mo (95%CI)	NR (9.7, NR)
mTTR, mo (95%CI)	1.4 (1.4, 1.5)

Progression-free survival

	n=87
Events, n	36
mPFS, mo (95%CI)	13.8 (9.7, NR)
Median follow-up, mo (95%CI)	11.1 (11.0, 13.7)



Organizado por:
GECP lung cancer research

Lu S, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA21.03

Novedades para pacientes CON diana accionable

RET

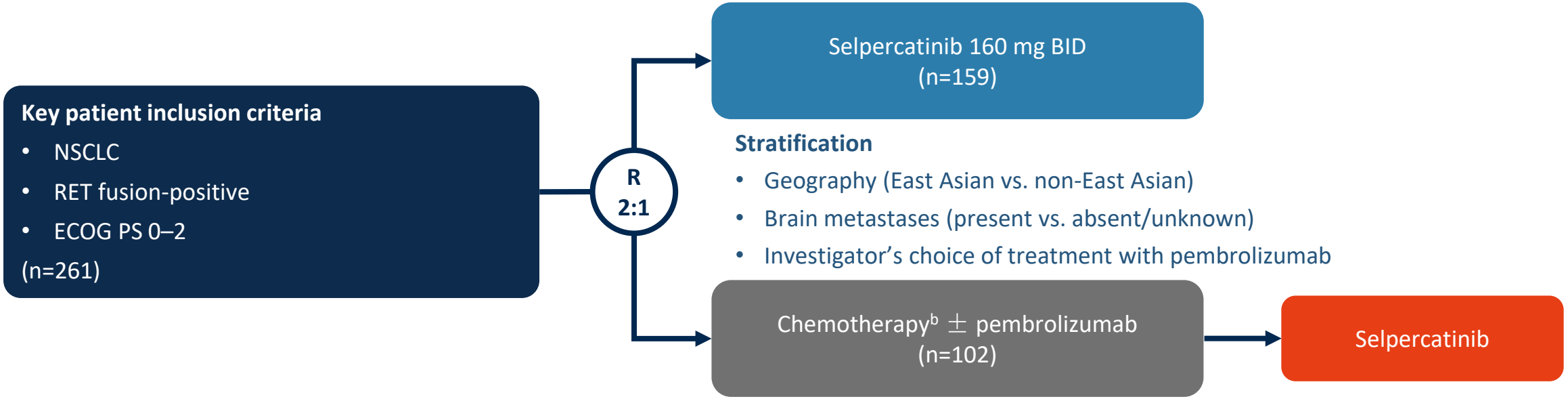
- LIBRETTO-431: **Selpercatinib** vs platino-pemetrexed-pembrolizumab (ESMO)

BRAF

- PHAROS: **Encorafenib + binimetinib** (ASCO)

RET: LIBRETTO-431

Randomized phase 3 study of first-line selpercatinib versus chemotherapy and pembrolizumab in RET fusion-positive NSCLC



Primary endpoint

- PFS (BICR)

Secondary endpoints

- OS, ORR, DoR, PROs, safety

Loong H, et al. Ann Oncol 2023;34(suppl):Abstr LBA4

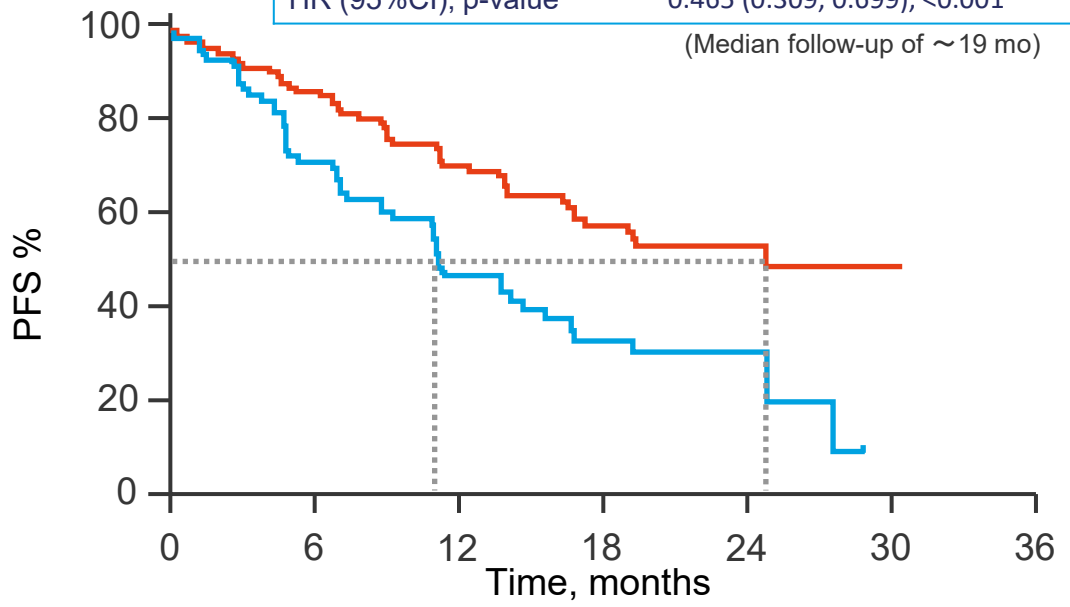
RET: LIBRETTO-431

Progression-free survival (BICR)

ITT-pembrolizumab population

	Selpercatinib (n=129)	Chemotherapy (n=83)
mPFS, mo (95%CI)	24.8 (16.9, NE)	11.2 (8.8, 16.8)
HR (95%CI); p-value	0.465 (0.309, 0.699), <0.001	

(Median follow-up of ~19 mo)



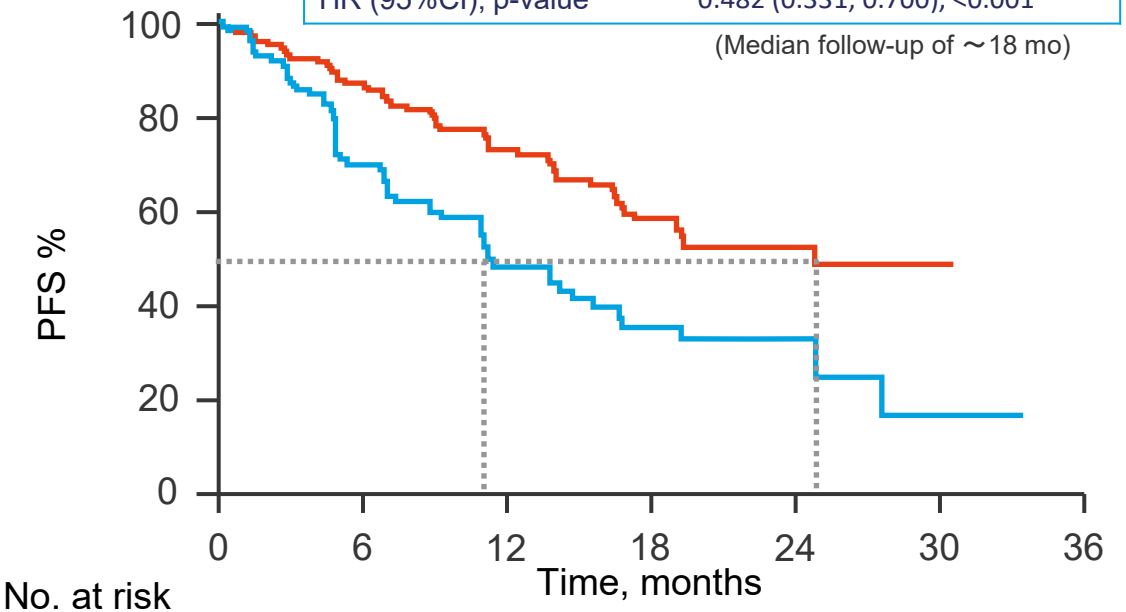
No. at risk

Selpercatinib	129	105	72	44	16	2	0
Control	83	55	29	15	6	0	0

ITT population

	Selpercatinib (n=159)	Chemotherapy (n=102)
mPFS, mo (95%CI)	24.8 (17.3, NE)	11.2 (8.8, 16.8)
HR (95%CI); p-value	0.482 (0.331, 0.700), <0.001	

(Median follow-up of ~18 mo)



No. at risk

Selpercatinib	159	130	90	52	18	3	0
Control	102	63	33	16	7	1	0

Organizado por: GECP lung cancer research

ESMO Congress 2023

Loong H, et al. Ann Oncol 2023;34(suppl):Abstr LBA4

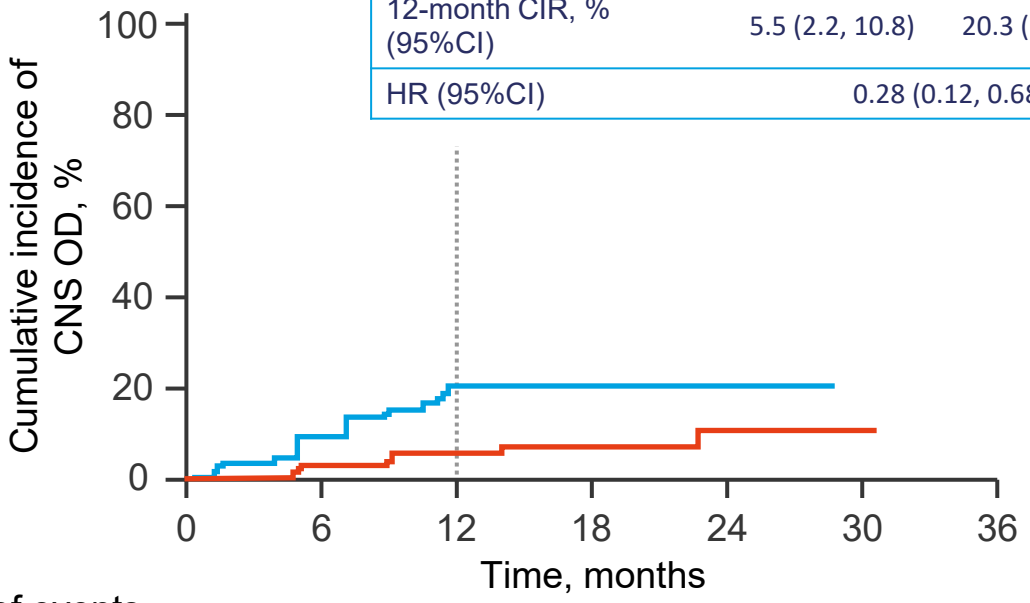
RET: LIBRETTO-431

Systemic outcomes[a]	Selpercatinib (n=129)	Chemotherapy (n=83)
ORR, %	83.7	65.1
mDoR, mo (95%CI)	24.2 (17.9, NE)	11.5 (9.7, 23.3)

Intracranial outcomes	Selpercatinib (n=17)	Chemotherapy (n=12)
Intracranial ORR, %	82.4	58.3
Intracranial CR, %	35.3	16.7
12-mo DoR rate, % (95%CI)	76.0 (42.2, 91.6)	62.5 (14.2, 89.3)
Median intracranial PFS, mo (95%CI)	16.1 (8.8, NE)	10.4 (3.8, NE)

Patients with and without baseline CNS metastases

	Selpercatinib	Chemotherapy
12-month CIR, % (95%CI)	5.5 (2.2, 10.8)	20.3 (11.3, 31.1)
HR (95%CI)	0.28 (0.12, 0.68)	



No. of events

Selpercatinib	0	3	6	7	8	8	8
Chemotherapy	0	6	13	13	13	13	13

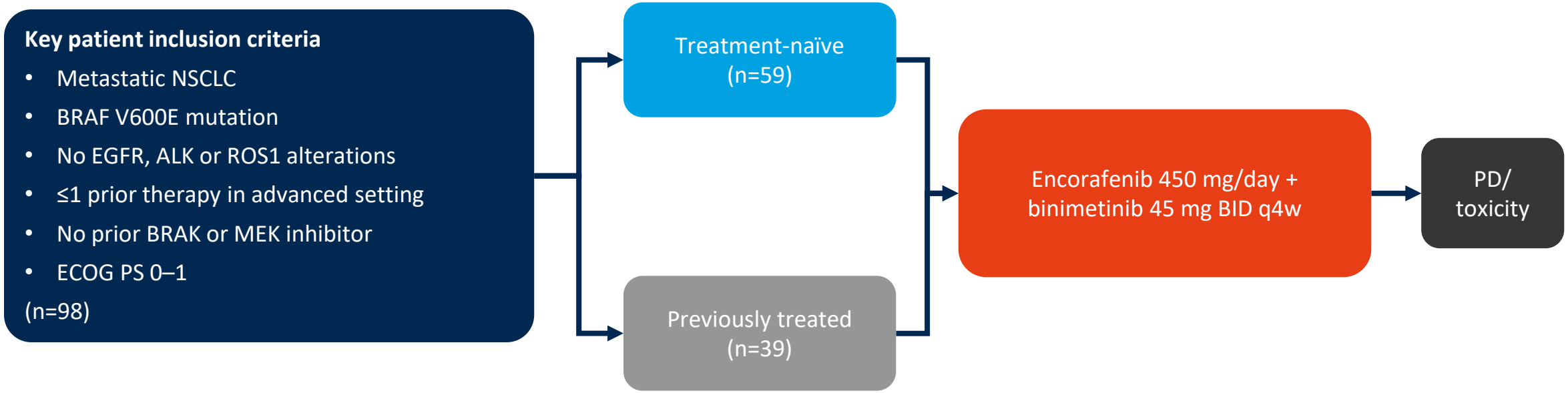
Organizado por: GECP lung cancer research

ESMO Congress 2023

Loong H, et al. Ann Oncol 2023;34(suppl):Abstr LBA4

BRAF: PHAROS

Efficacy and safety of encorafenib plus binimetinib in patients with BRAF V600E-mutant (BRAFV600E) metastatic non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study



Primary endpoint

- ORR (IRR)

Secondary endpoints

- DoR, DCR, PFS, TTR, OS, safety

Riely GJ, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9018

BRAF: PHAROS

Response	Treatment-naïve (n=59)	Previously treated (n=39)
ORR,[a] % (95%CI)	75 (62, 85)	46 (30, 63)
BOR, n (%)		
CR	9 (15)	4 (10)
PR	35 (59)	14 (36)
SD	10 (17)	13 (33)
PD	2 (3)	3 (8)
DCR at 24 weeks, % (95%CI)	64 (51, 76)	41 (26, 58)
mDoR, mo (95%CI)	NE (23.1, NE)	16.7 (7.4, NE)
Duration of response ≥12 months, n/N (%)	26/44 (59)	6/18 (33)
mTTR, mo (range)	1.9 (1.1–19.1)	1.7 (1.2–7.3)
PFS events, n (%)	21 (36)	17 (44)
mPFS, mo (95%CI)	NE (15.7, NE)	9.3 (6.2, NE)

Riely GJ, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9018

BRAF: PHAROS

Response	Treatment-naïve (n=59)	Previously treated (n=39)
ORR,[a] % (95%CI)	75 (62, 85)	46 (30, 63)
BOR, n (%)		
CR	9 (15)	4 (10)
PR	35 (59)	14 (36)
SD	10 (17)	13 (33)
PD	2 (3)	3 (8)
DCR at 24 weeks, % (95%CI)	64 (51, 76)	41 (26, 58)
mDoR, mo (95%CI)	NE (23.1, NE)	16.7 (7.4, NE)
Duration of response ≥12 months, n/N (%)	26/44 (59)	6/18 (33)
mTTR, mo (range)	1.9 (1.1–19.1)	1.7 (1.2–7.3)
PFS events, n (%)	21 (36)	17 (44)
mPFS, mo (95%CI)	NE (15.7, NE)	9.3 (6.2, NE)

Riely GJ, et al. J Clin Oncol 2023;41(suppl 16):Abstr 9018

CAMBIOS RELEVANTES EN PRÁCTICA CLÍNICA ASISTENCIAL?

Novedades para pacientes sin diana accionable

- 1aL **Nivo+Ipi+QT**: pensar en pacientes con PD-L1 negativo y/o carcinoma escamoso y/o para ahorrar toxicidad por quimioterapia
- Progresión a QT-IT CPNCP no escamoso: a la espera de SG Datopotamab-DTX

Novedades para pacientes con diana accionable

- 1aL EGFR: debate futuro Osimertinib vs **Osi+QT** vs **Amivantanab+Lazertinib**
  i. Pacientes jóvenes con afectación SNC → Osi+QT
  ii. Pacientes con buen estado general→ Amivantanab/Lazertinib
  iii. Edad avanzada y/o unfit → Osimertinib monoterapia
- 2aL EGFR: a la progresión a Osimertinib: **Amivantanab+QT**
- Añadir inmunoterapia en pacientes EGFR o ALK: **no beneficio aparente**

Organizado por:
GECP lung cancer research

CAMBIOS RELEVANTES EN PRÁCTICA CLÍNICA ASISTENCIAL?

Novedades para pacientes con diana accionable

- EGFR ins20: **Amivantanab + QT** vs ensayos clínicos prometedores
- Fusión de RET: **Selpercatinib**
- BRAF V600E: Solicitar uso compasivo para doble inhibición como Encorafenib + Binimetinib

MUCHAS GRACIAS

Pico Mulleres, 3013m, cara sur-este, 13.1.2024