Universiteit Antwerpen

UZA

POST ASCO 2025

TOGA vergadering

woensdag 18 juni 2025

2025 ASCO ANNUAL MEETING

#ASCO25

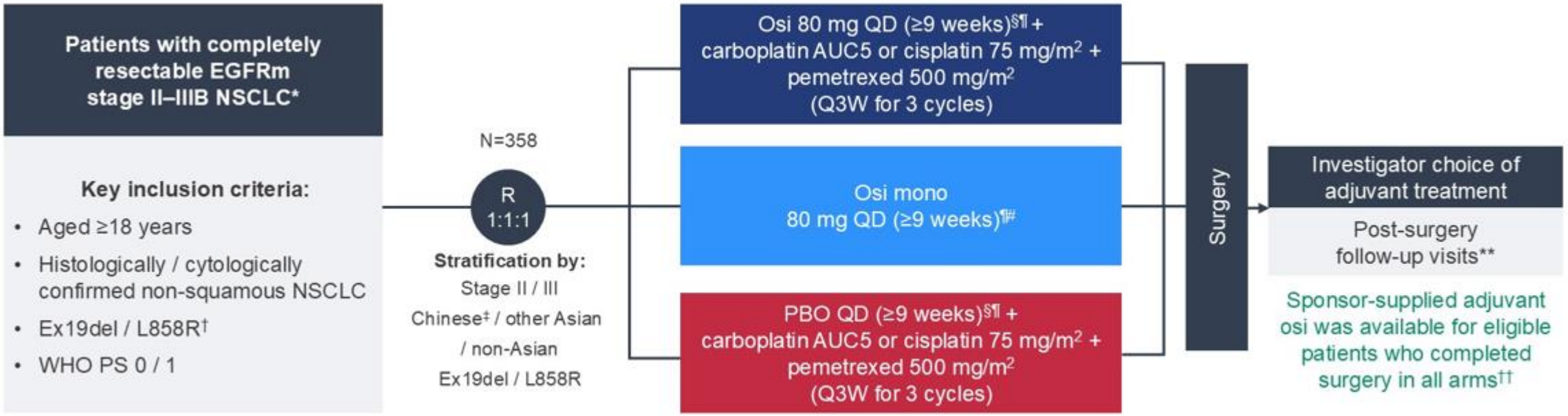
PRESENTED BY: Jo Raskin MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

KNOWLEDGE CONQUERS CANCER

EGFR / ALK
non metastatic

NEOADAURA



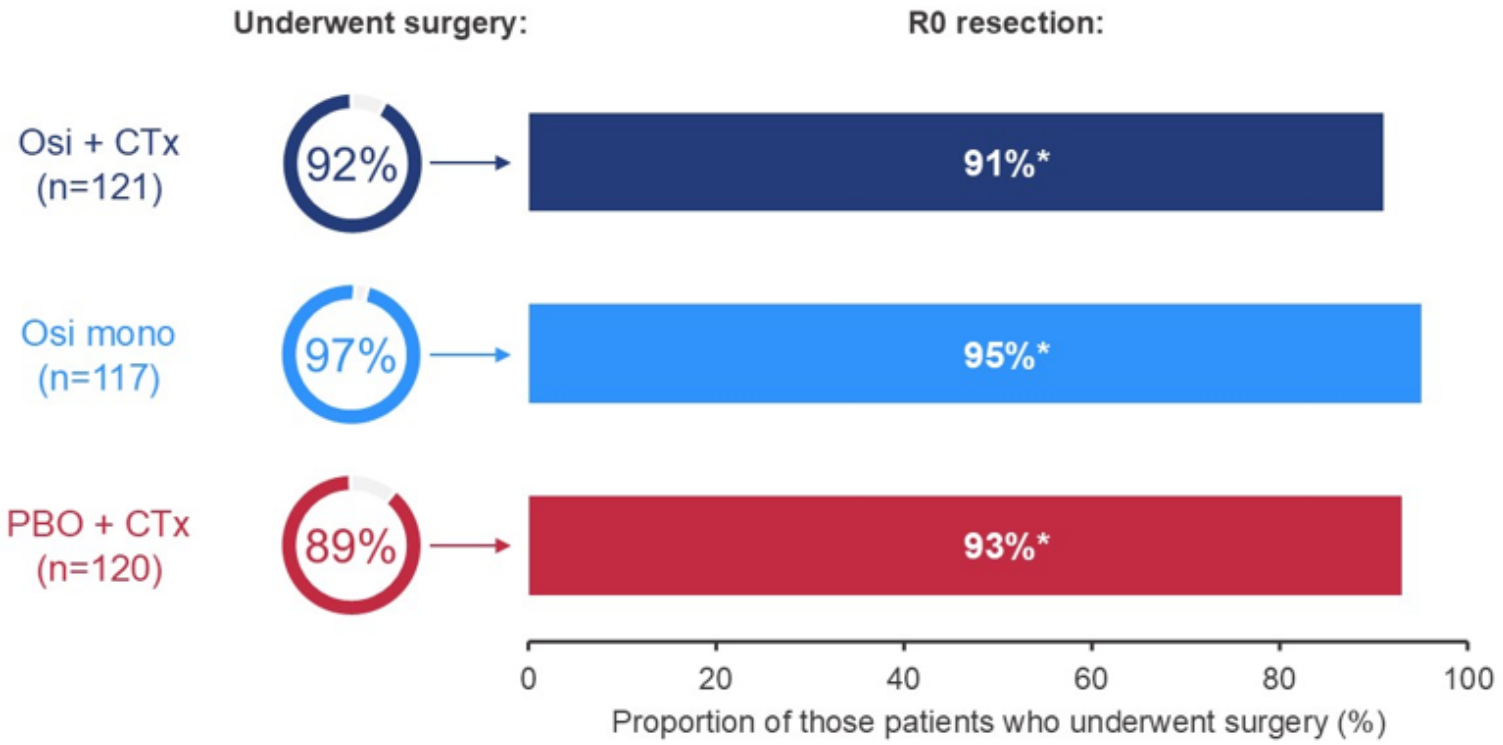
Chaft JE. ASCO 2025

NEOADAURA

Characteristic, %	Osi + CTx (n=121)	Osi mono (n=117)	PBO + CTx (n=120)
Sex: male / female	40 / 60	35 / 65	25 / 75
Age: median (range), years	63 (31–82)	66 (42–83)	65 (36–86)
Smoking history: former or current / never	32 / 68	34 / 66	22 / 78
Race:* Chinese† / other Asian / non-Asian	24 / 49 / 27	23 / 50 / 26	26 / 49 / 25
WHO PS: 0 / 1	80 / 20	79 / 21	83 / 17
Histology: adenocarcinoma / other	98 / 2	100 / 0	100 / 0
EGFR mutation at randomization:* Ex19del / L858R	50 / 50	51 / 49	51 / 49
AJCC staging (8th edition) at diagnosis:* II / III	49 / 51	50 / 50	51 / 49
Regional lymph nodes: N0 / N1 / N2	26 / 35 / 39	26 / 38 / 35	29 / 37 / 34
Baseline tumor size, mean (SD), cm	4.2 (1.4)	4.0 (1.5)	4.3 (1.6)

Chaft JE. ASCO 2025

NEOADAURA



In each arm, **91%** of patients who completed surgery received sponsor-supplied adjuvant osi†

Chaft JE. ASCO 2025

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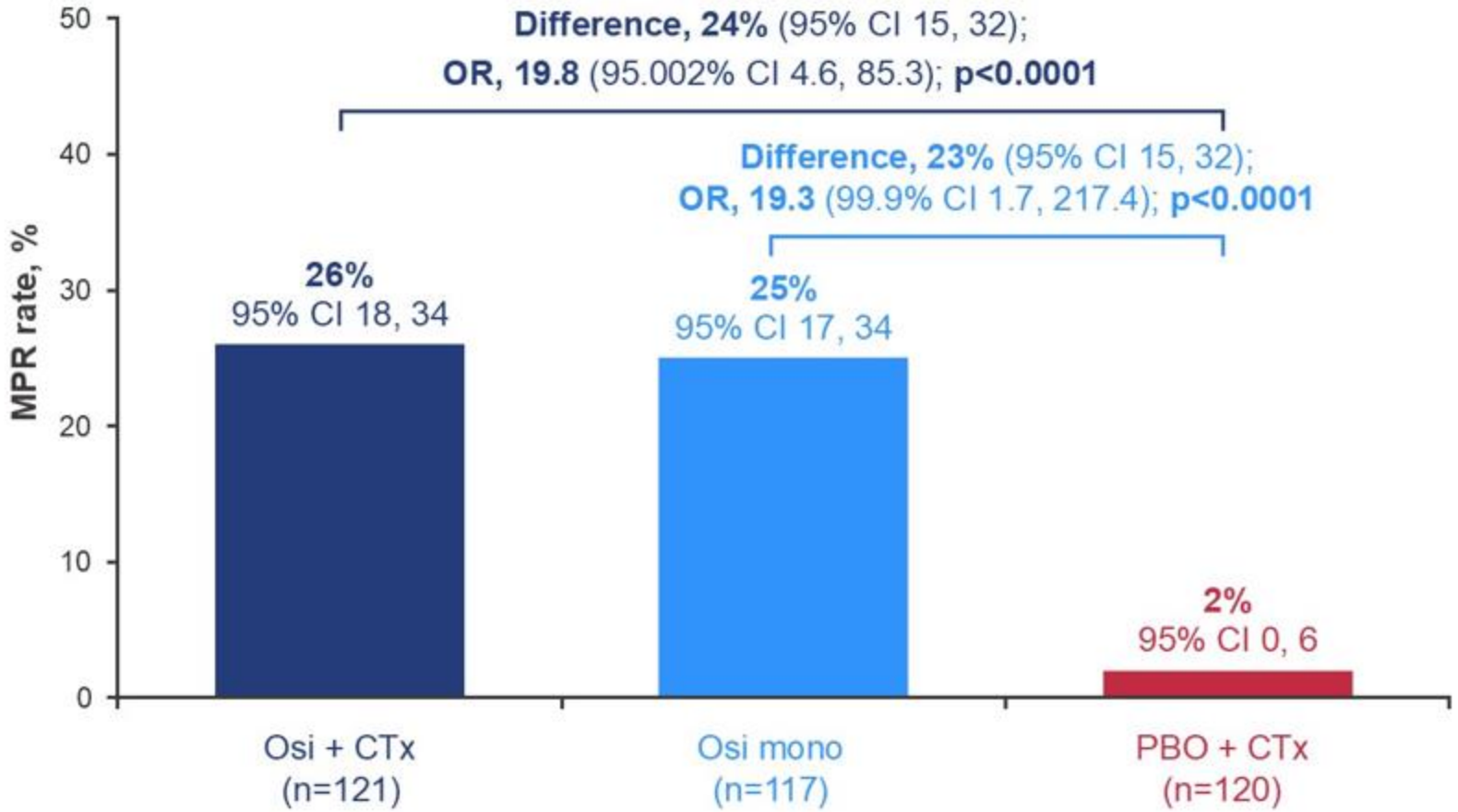

Chaft JE. ASCO 2025

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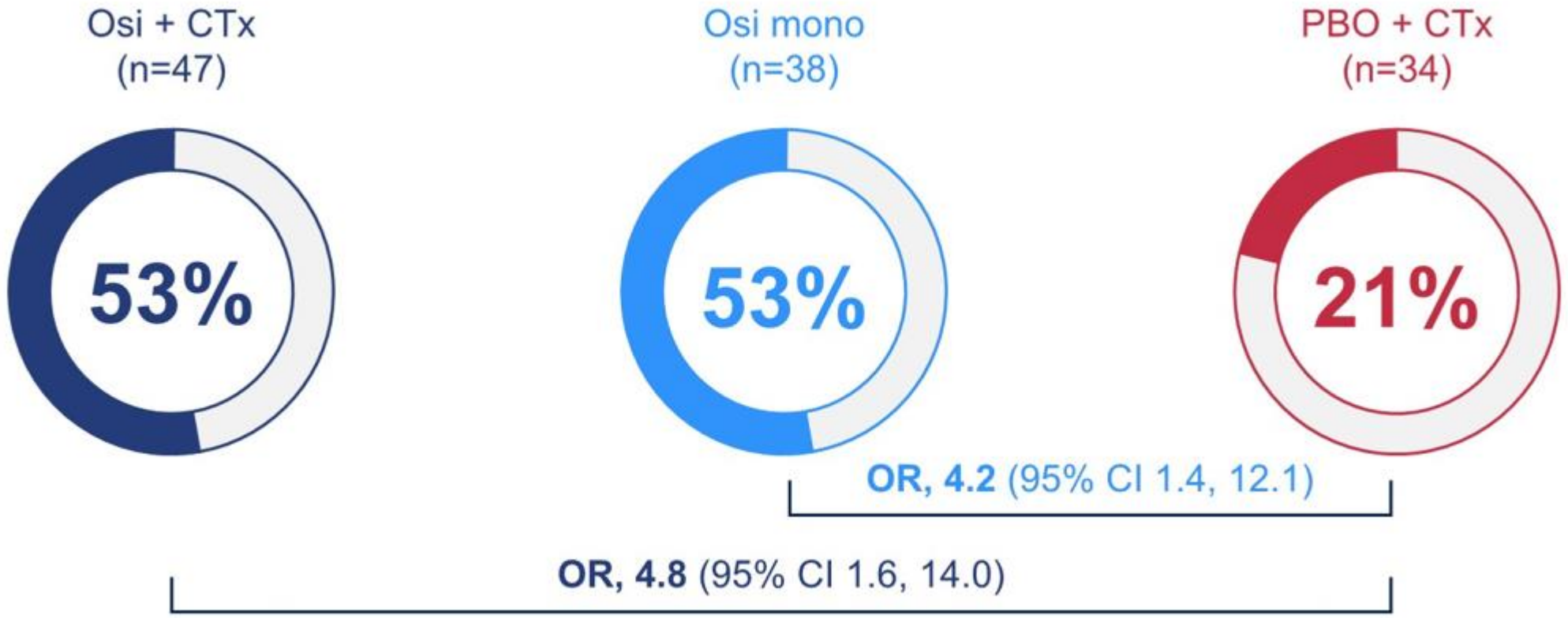

nodal downstaging

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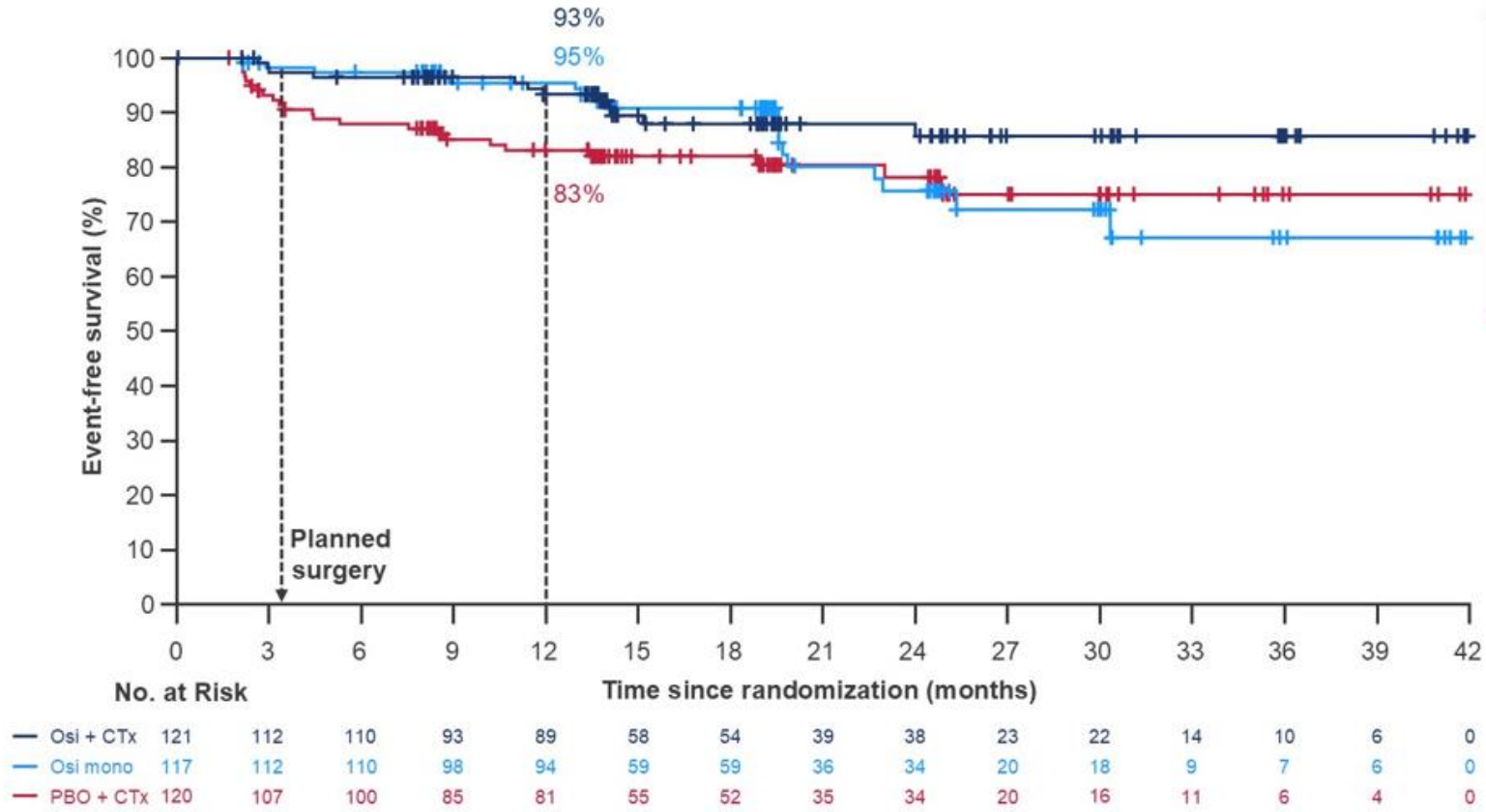
NEOADAURA

Interim EFS analysis (15% maturity)



EFS HR vs PBO + CTx

Osi + CTx: 0.50
(99.8% CI 0.17, 1.41); p=0.0382†

Osi mono: 0.73
(95% CI 0.40, 1.35)†

Median follow-up, months‡
osi + CTx 14.3, osi mono 18.3,
PBO + CTx 14.3

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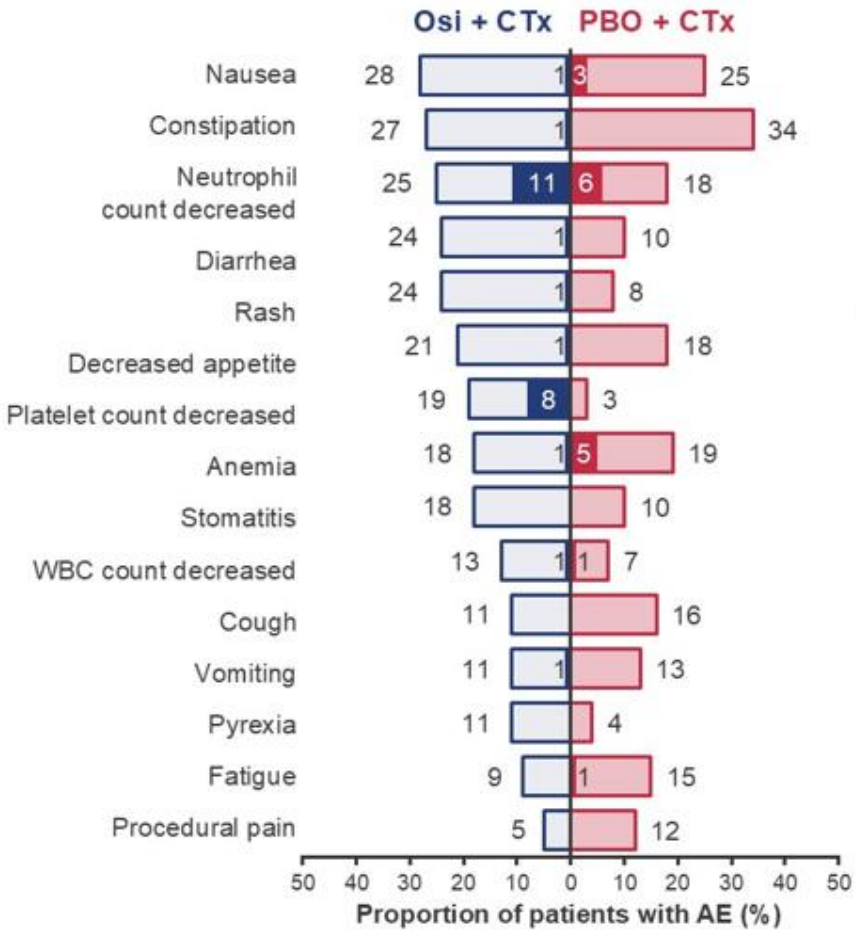
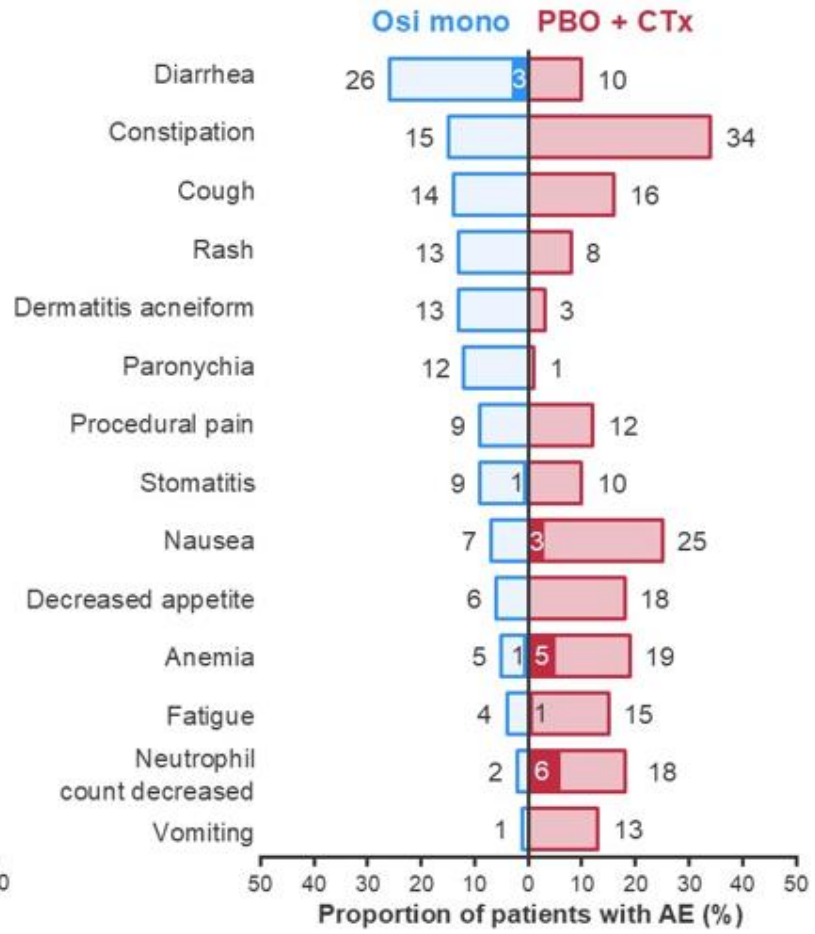
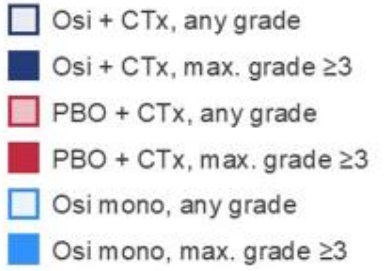
NEOADAURA





AESI, n (%)	Osi + CTx (n=119)	PBO + CTx (n=120)	Osi mono (n=117)
Wound complications	2 (2)	0	1 (1)
Cardiac effects	1 (1)	2 (2)	3 (3)
ILD / pneumonitis	0	0	2 (2)



Chaft JE. ASCO 2025

ALNEO

- Resectable locally advanced stage III NSCLC
- Candidate for surgical resection after multidisciplinary discussion
- ALK-positive (IHC/FISH/NGS)
- No Previous treatment
- ECOG PS 0-1

Primary Endpoint: MPR (≤10% viable tumor) by BICR

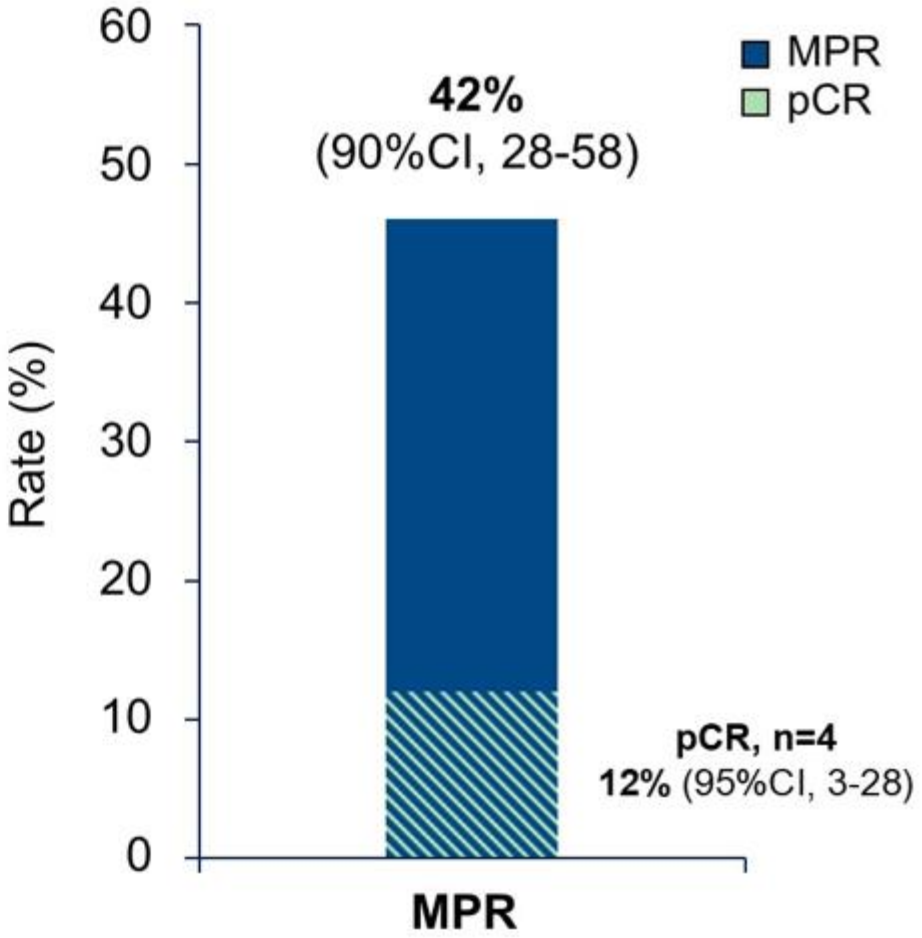
Secondary Endpoints: pCR by BICR, ORR, EFS, DFS, OS, AEs

Tiseo M. ASCO 2025

ALNEO

Pathologic Response	N=33
MPR (≤10% viable tumor), n (%)	14 (42)
Non-MPR (>10% viable tumor), n (%)	13 (40)
Not assessed, n (%)	6 (18)[a]

[a]5 patients did not undergo surgery, 1 patient underwent explorative thoracotomy

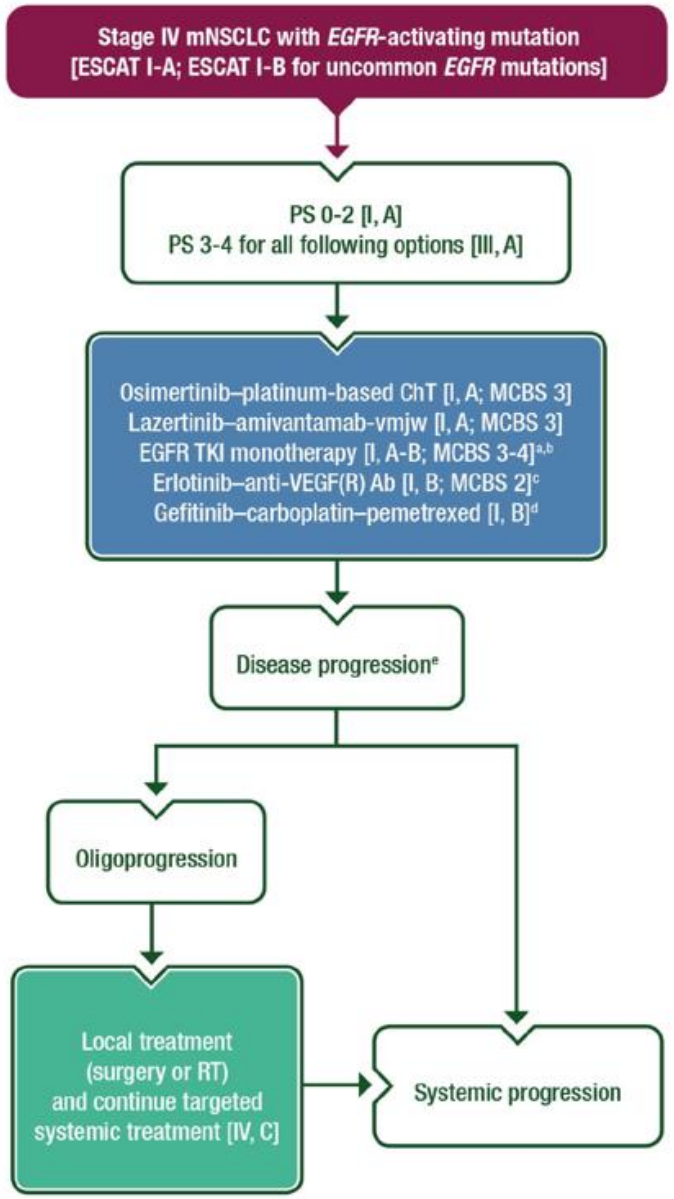


Tiseo M. ASCO 2025

EGFR metastatic

CLINICAL PRACTICE GUIDELINES

ESMO Oncogene-Addicted Metastatic Non-Small-Cell Lung Cancer Living Guideline
v1.2 January 2025



FLAURA2
Planchard D. N Engl J Med 2023

ORR 83%
mPFS 25.5 m
mOS NR (>38 m)
TRAE G≥3 64%

MARIPOSA
Cho BC. N Engl J Med 2024

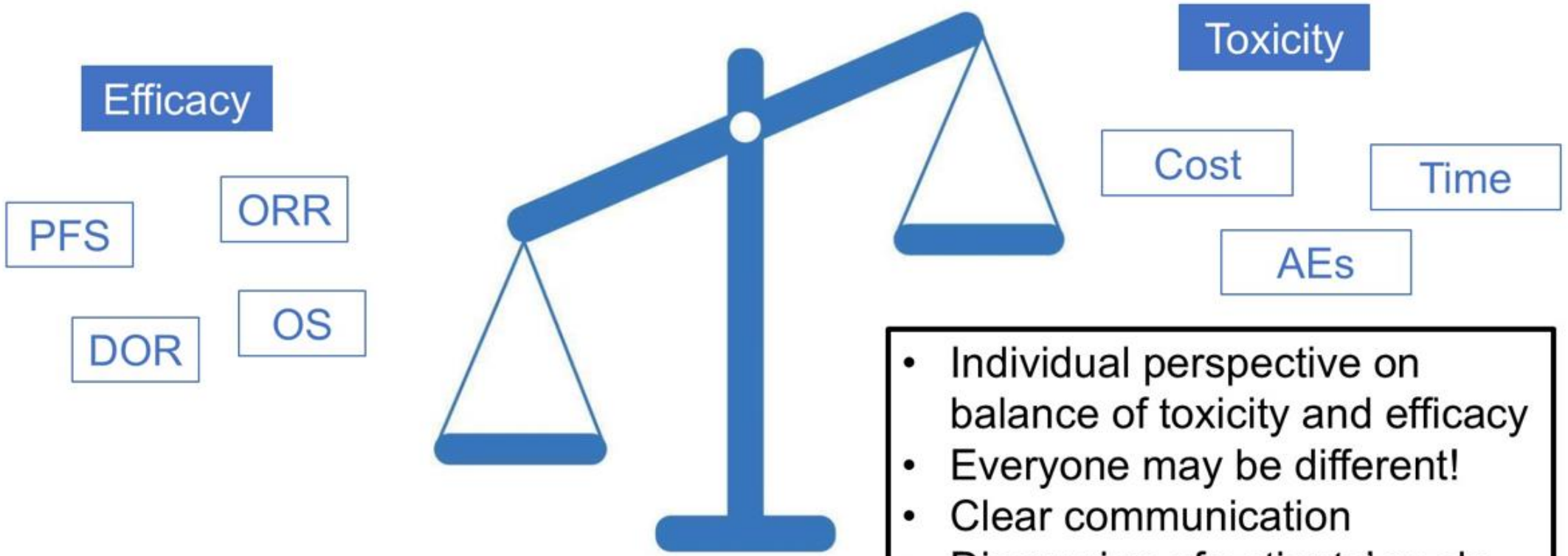
ORR 86%
mPFS 23.7 m
mOS NR (>43 m)
TRAE G≥3 ?

FLAURA
Soria J-C. N Engl J Med 2018
ORR 80%
mPFS 18.9 m
mOS 38.6 m
TRAE G≥3 34%

RELAY
Nakagawa K. Lancet 2019

ORR 76%
mPFS 19.4 m
mOS 51.1 m [NS]
TRAE G≥3 72%

SELECTION OF 1L TREATMENT



- Individual perspective on balance of toxicity and efficacy
- Everyone may be different!
- Clear communication
- Discussion of patients' goals and values

Bauman J. ASCO 2025

ESMO Oncogene-Addicted Metastatic Non-Small-Lung Cancer Living Guideline
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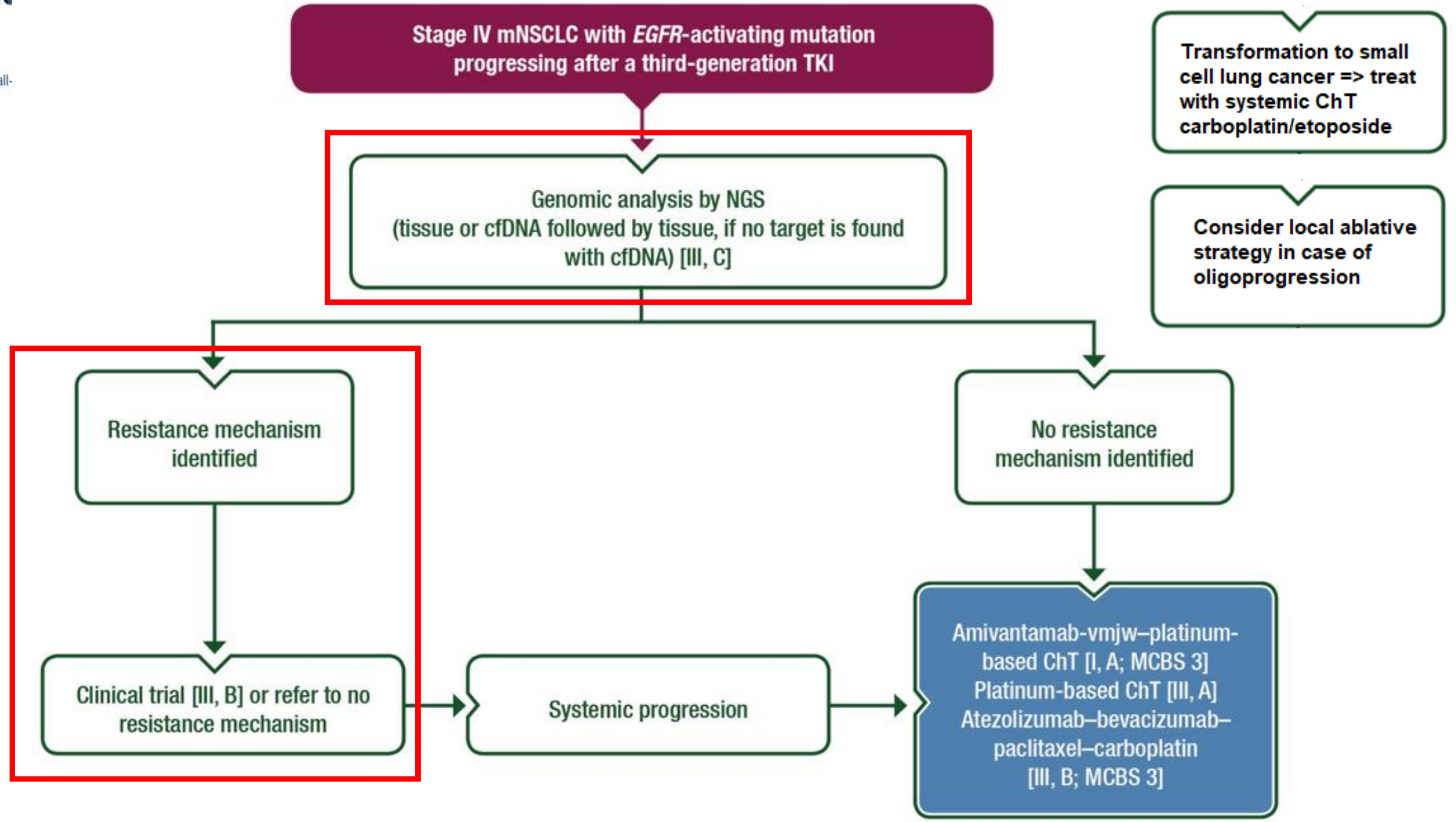
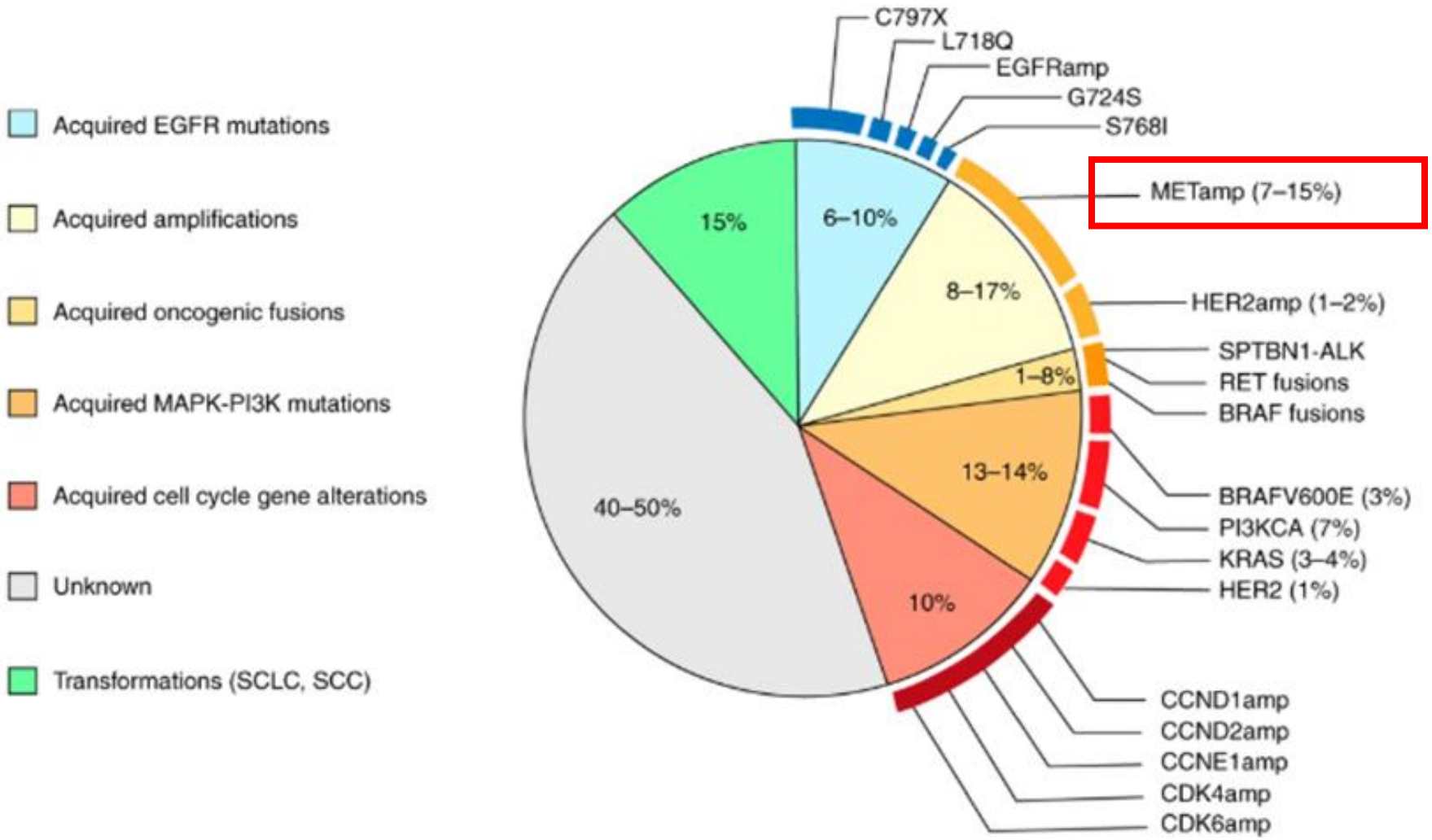
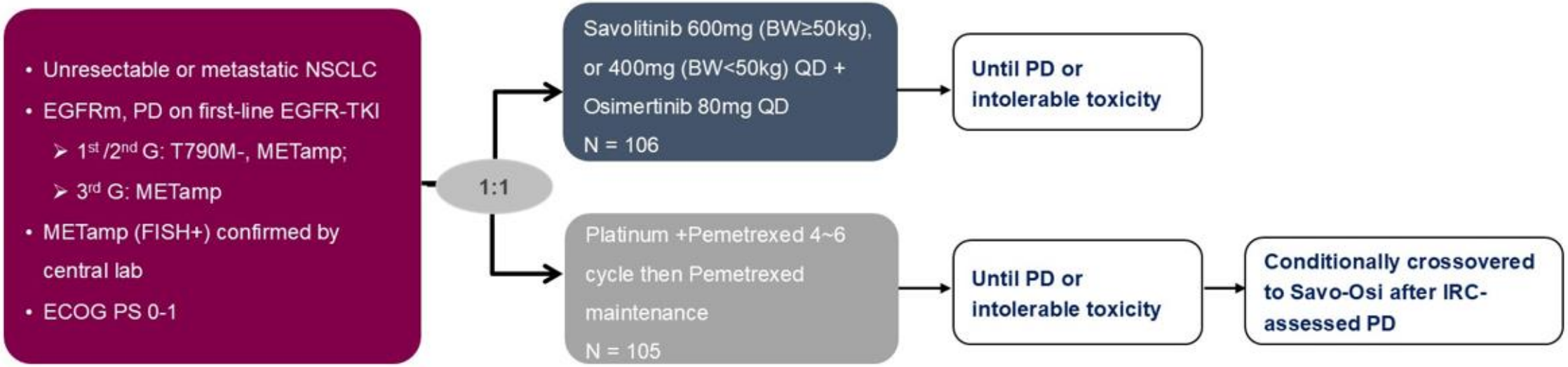


RESISTANCE TO OSIMERTINIB 1L



Leonetti A. Br J Cancer 2019

SACHI



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)

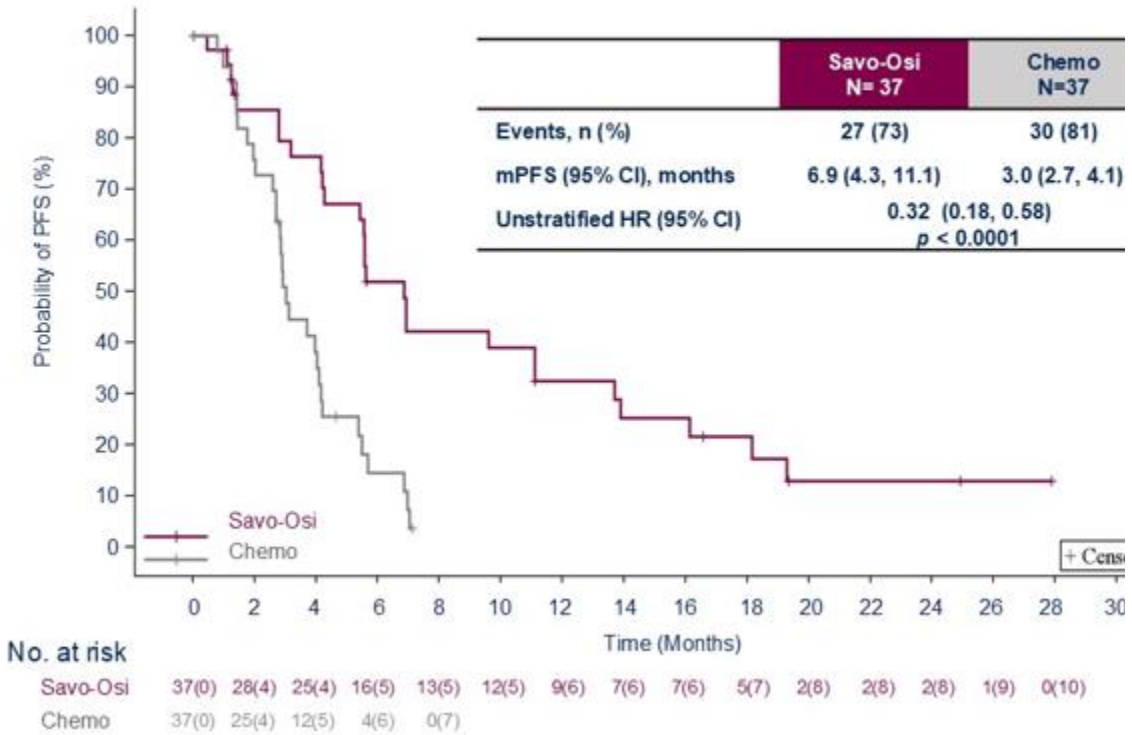
Primary endpoint: PFS by investigator

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

Lu S. ASCO 2025

SACHI

IRC

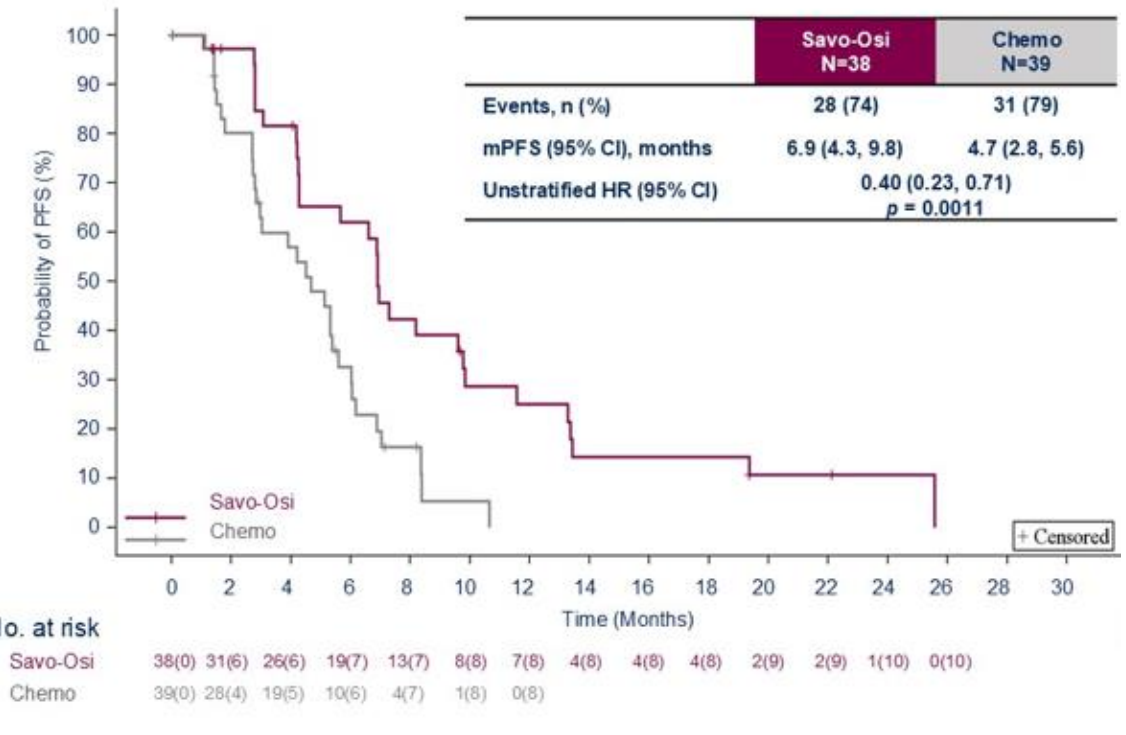


	Savo-Osi N= 37	Chemo N=37
Events, n (%)	27 (73)	30 (81)
mPFS (95% CI), months	6.9 (4.3, 11.1)	3.0 (2.7, 4.1)
Unstratified HR (95% CI)	0.32 (0.18, 0.58) $p < 0.0001$	

No. at risk

Savo-Osi	37(0)	28(4)	25(4)	16(5)	13(5)	12(5)	9(6)	7(6)	7(6)	5(7)	2(8)	2(8)	2(8)	1(9)	0(10)
Chemo	37(0)	25(4)	12(5)	4(6)	0(7)										

With history of brain metastases



	Savo-Osi N=38	Chemo N=39
Events, n (%)	28 (74)	31 (79)
mPFS (95% CI), months	6.9 (4.3, 9.8)	4.7 (2.8, 5.6)
Unstratified HR (95% CI)	0.40 (0.23, 0.71) $p = 0.0011$	

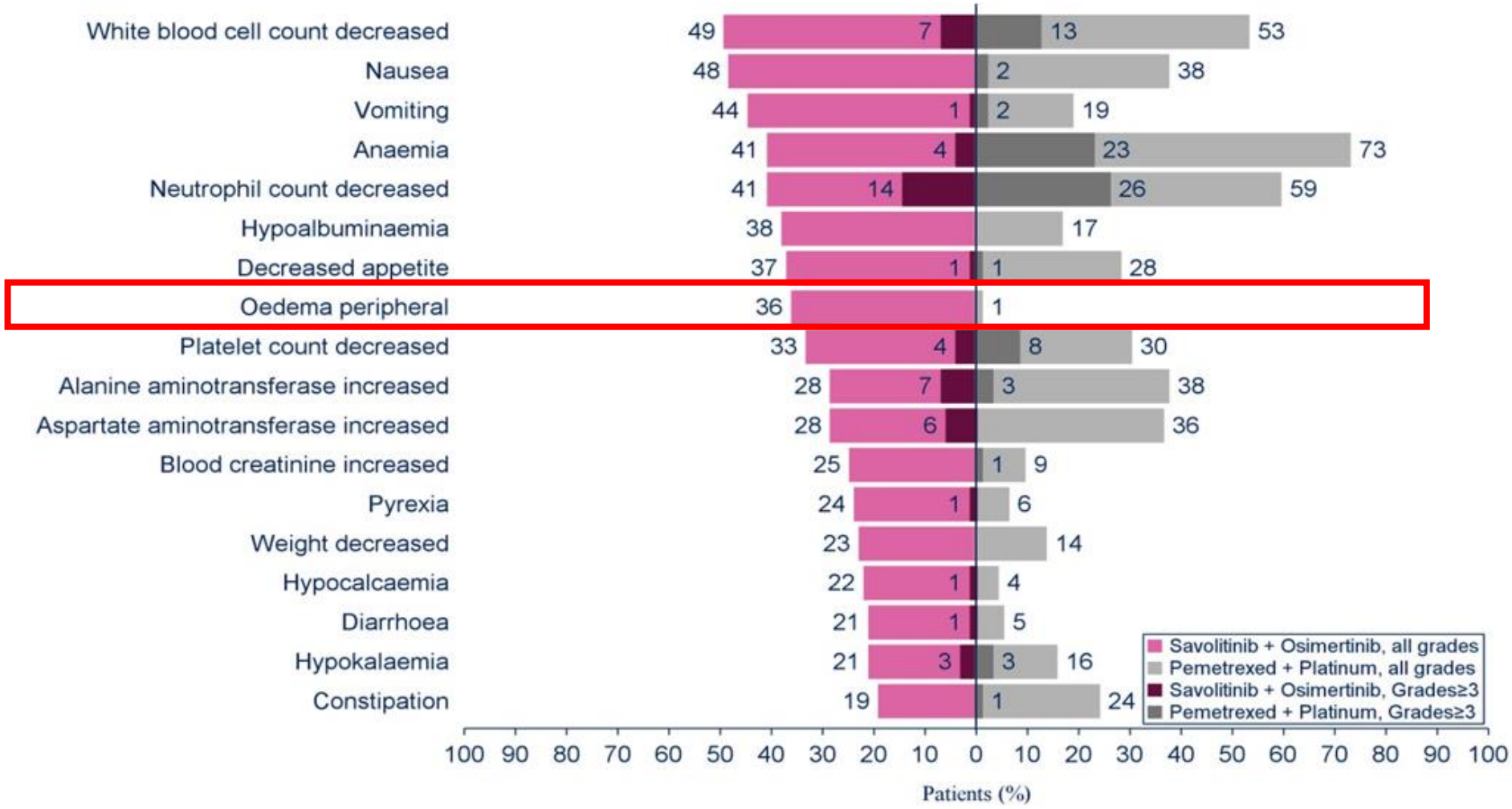
No. at risk

Savo-Osi	38(0)	31(6)	26(6)	19(7)	13(7)	8(8)	7(8)	4(8)	4(8)	4(8)	2(9)	2(9)	1(10)	0(10)	
Chemo	39(0)	28(4)	19(5)	10(6)	4(7)	1(8)	0(8)								

	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)	-

Lu S. ASCO 2025

SACHI



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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

Noronha V. ASCO 2025

MET-TKIs

Name	Design	Number of patients	Inclusion criteria	Endpoints	Results
INSIGHT2	Phase 2 study of osimertinib + tepotinib	128	EGFRm NSCLC, PD on 1st line Osimertinib, with METamp	1º: ORR 2º: PFS, OS, DoR, QoL	ORR: 50% mPFS: 5.6 mths mOS: 17.8 mths Grade ≥ 3 AEs: 38.9%
GEOMETRY mono-1	Phase 2 study of capmatinib	Total 364 (100 were previously treated)	Multiple cohorts	1º: ORR 2º: PFS, OS, DoR, QoL	ORR: 29% in previously treated with METamp mPFS: 4.1 mths; Grade ≥ 3 AEs: 44%

Noronha V. ASCO 2025

CLINICAL PRACTICE GUIDELINES

ESMO Oncogene-Addicted Metastatic Non-Small-Cell Lung Cancer Living Guideline
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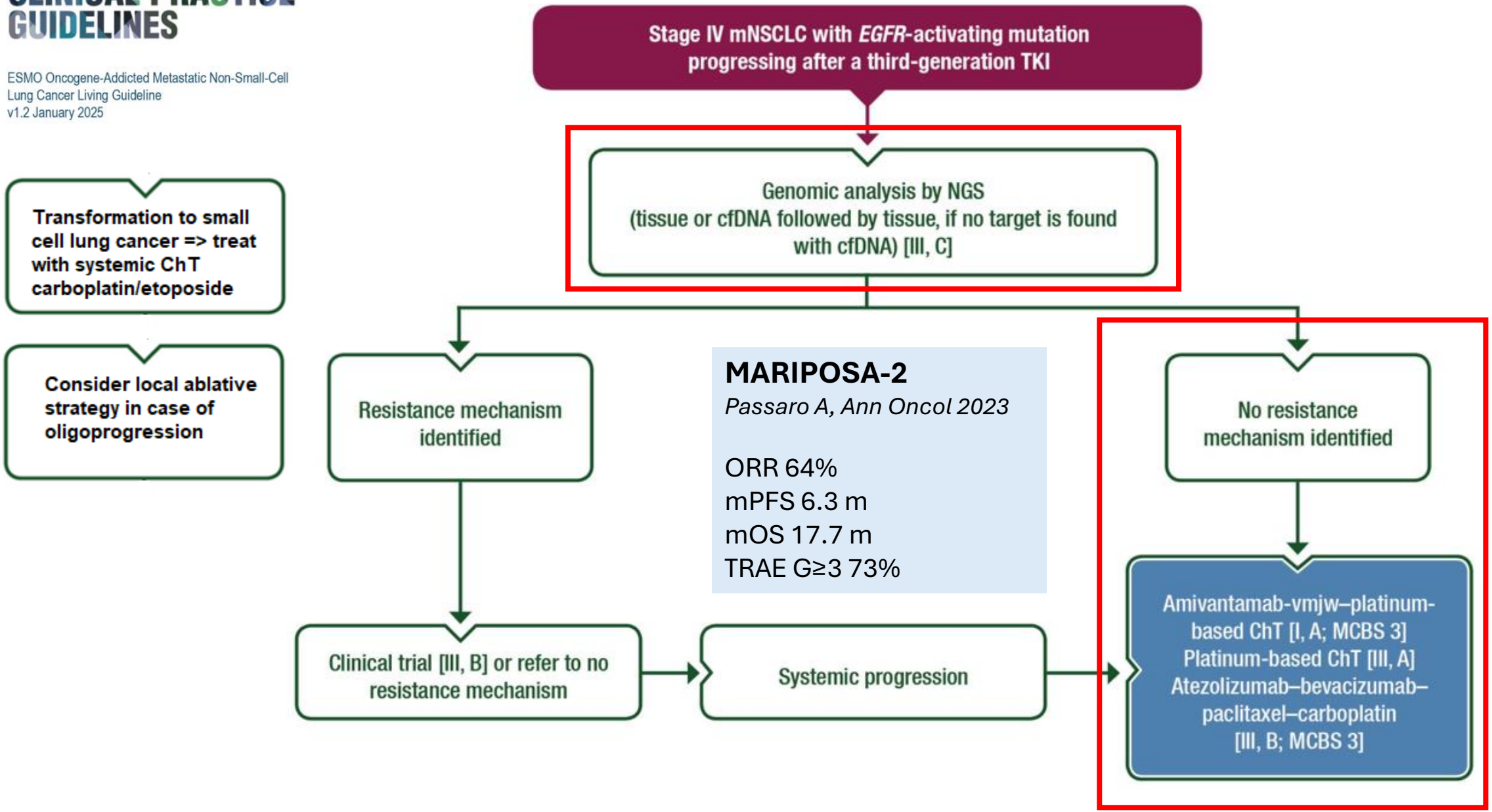


MARIPOSA-2
Passaro A, Ann Oncol 2023

ORR 64%
mPFS 6.3 m
mOS 17.7 m
TRAE G≥3 73%

No resistance mechanism identified

Amivantamab-vmjw–platinum-based ChT [I, A; MCBS 3]
Platinum-based ChT [III, A]
Atezolizumab–bevacizumab–paclitaxel–carboplatin [III, B; MCBS 3]

Ivonescimab-platinum based ChT (HARMONi-A)

~~Patritumab-deruxtecan [HERTHENA-Lung02]~~

586 patients; study start date, 08 July 2022

Select Eligibility Criteria

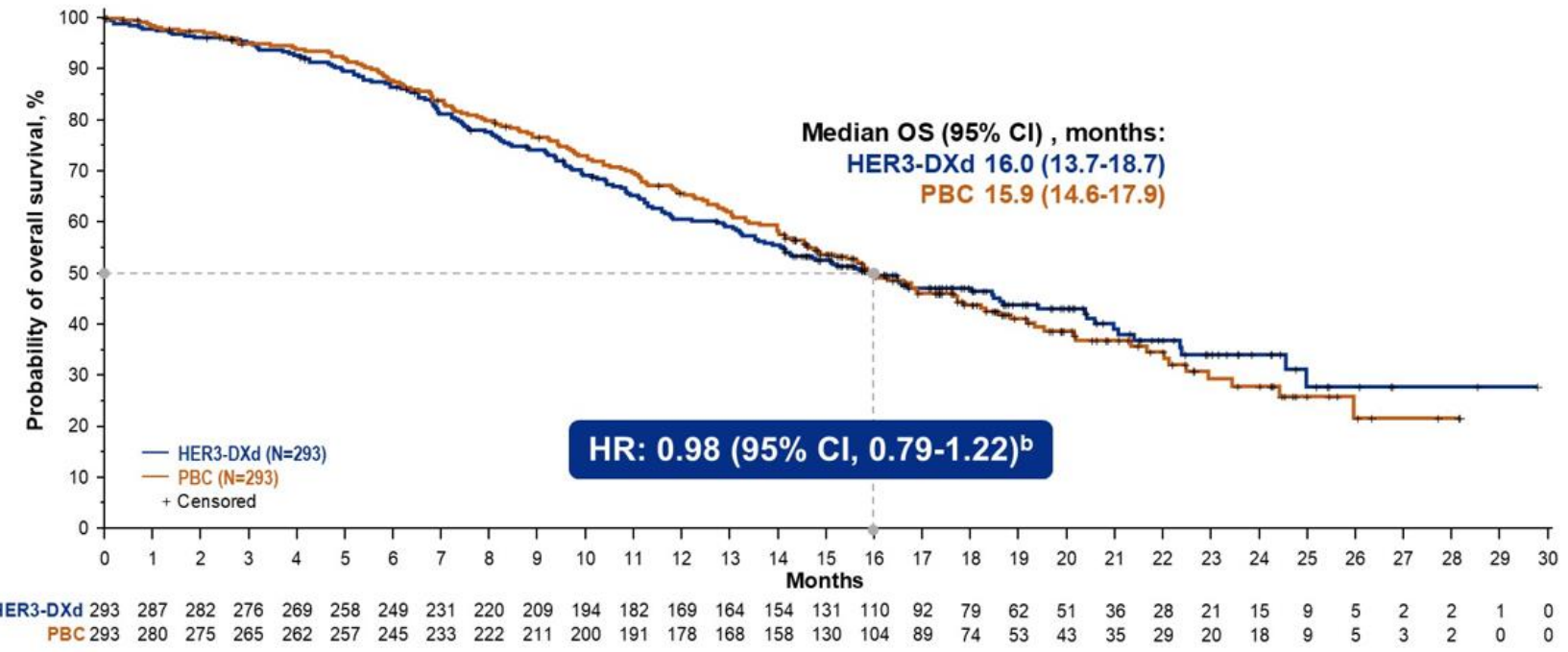
- Advanced nonsquamous NSCLC with an *EGFR*-activating mutation (exon 19 deletion or L858R)
- 1 or 2 prior line(s) of an approved EGFR TKI (must include a third-generation EGFR TKI)
  - Non-osimertinib third-generation TKIs ≤20% in each arm
- Disease progression while or after receiving a third-generation EGFR TKI
- Stable brain metastases (asymptomatic and not requiring corticosteroids or anticonvulsants) were permitted

Randomized 1:1

HER3-DXd (N=293)
Patritumab deruxtecan 5.6 mg/kg IV Q3W

No crossover

PBC (N=293)
Cisplatin 75 mg/m^2 *or* carboplatin AUC5 Q3W (× 4 cycles) + Pemetrexed 500 mg/m^2 Q3W[a]



Mok TSK. ASCO 2025

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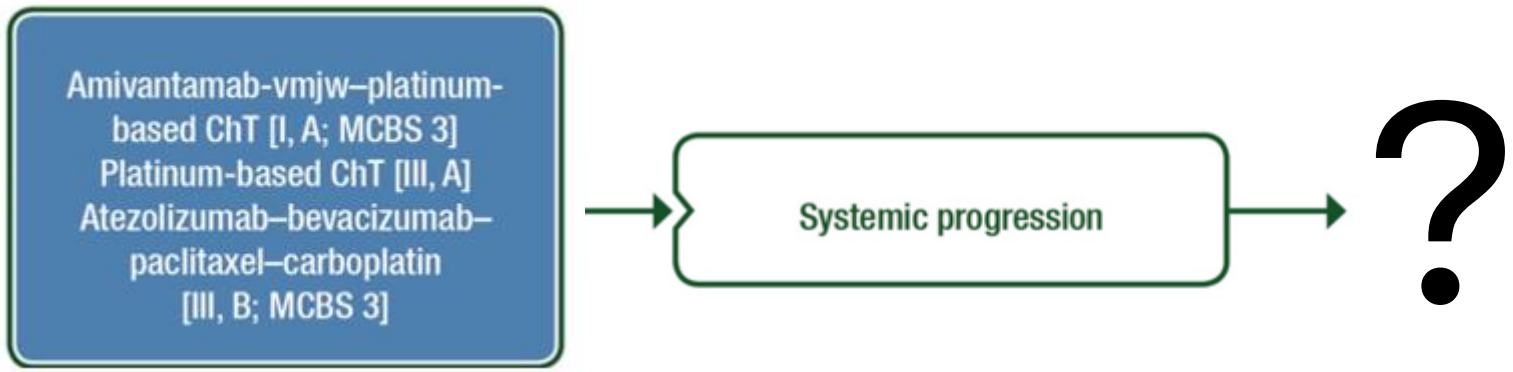
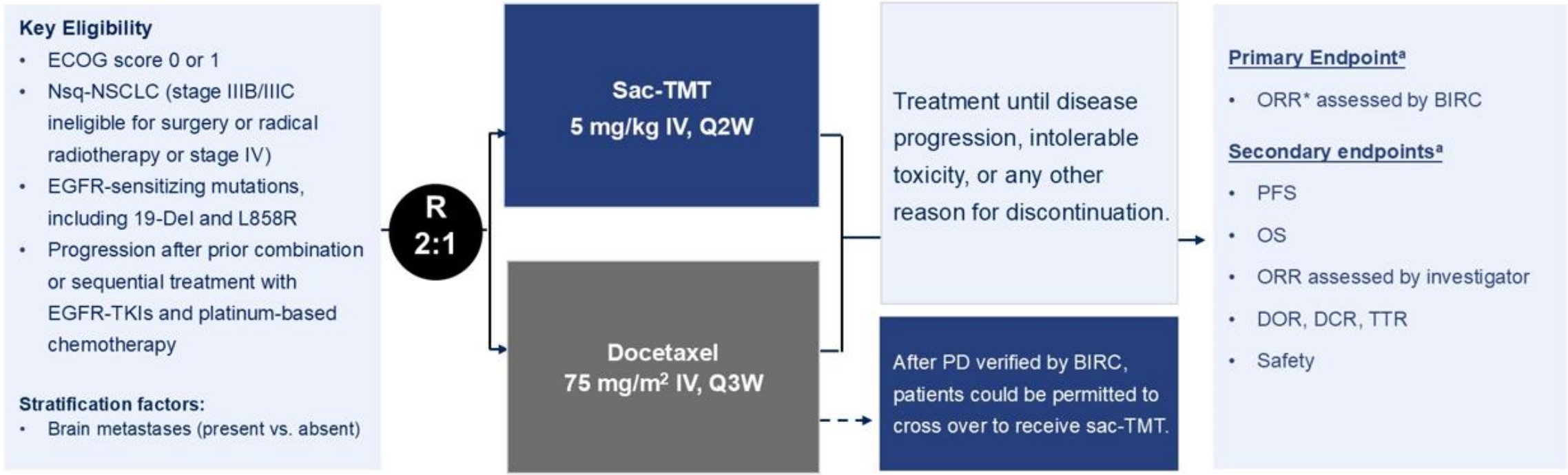


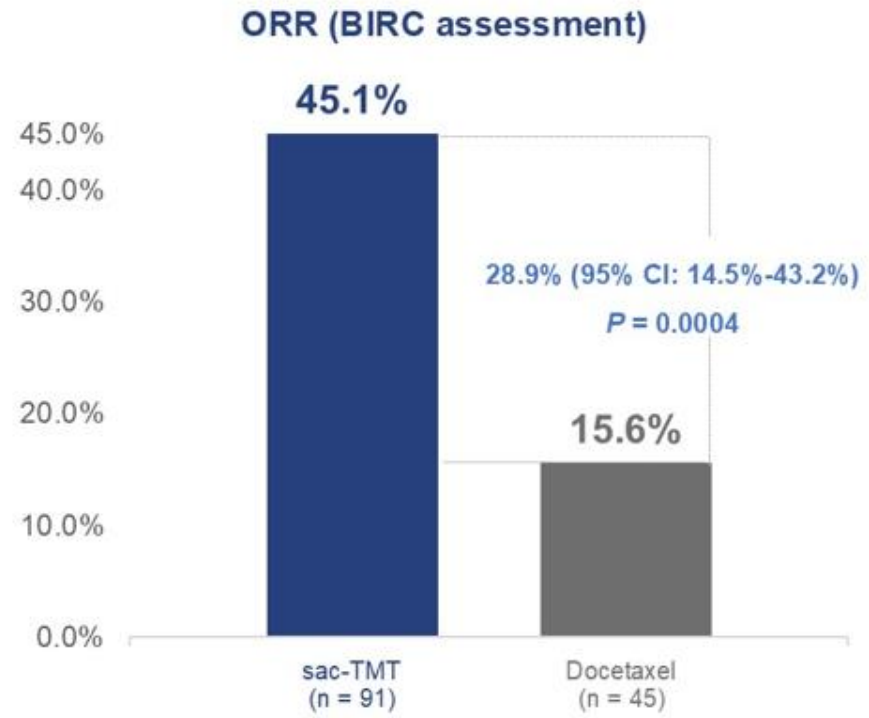
OPTITROP-LUNG03



Zhang L. ASCO 2025

OPTITROP-LUNG03

	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)



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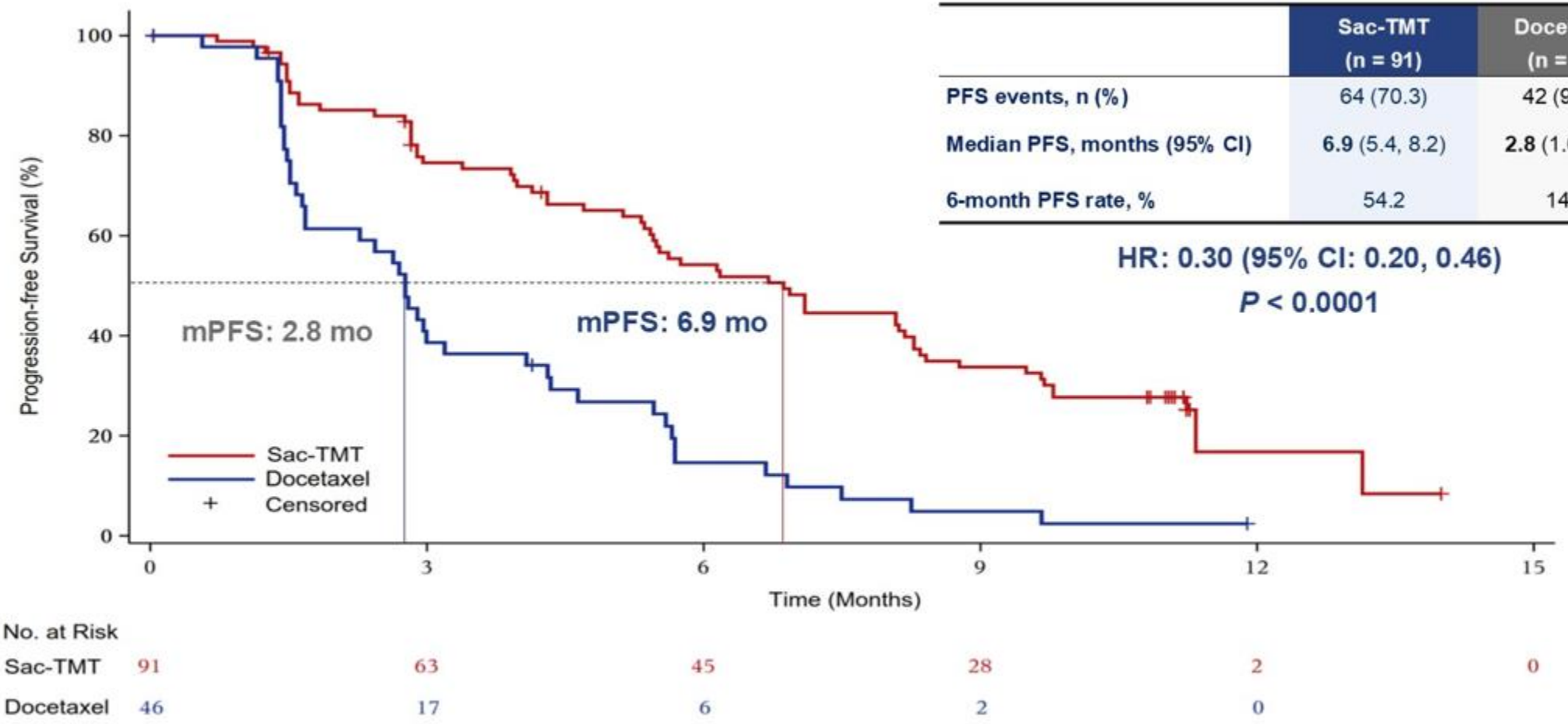
OPTITROP-LUNG03



	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**

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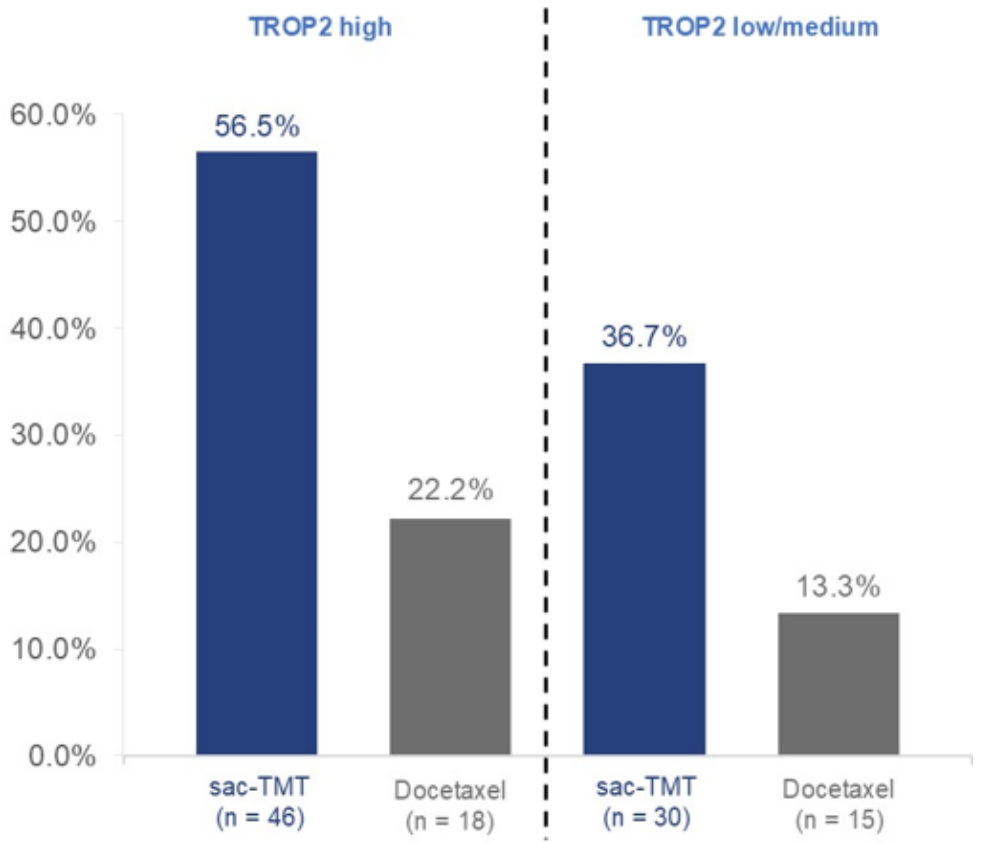
OPTITROP-LUNG03

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)**	



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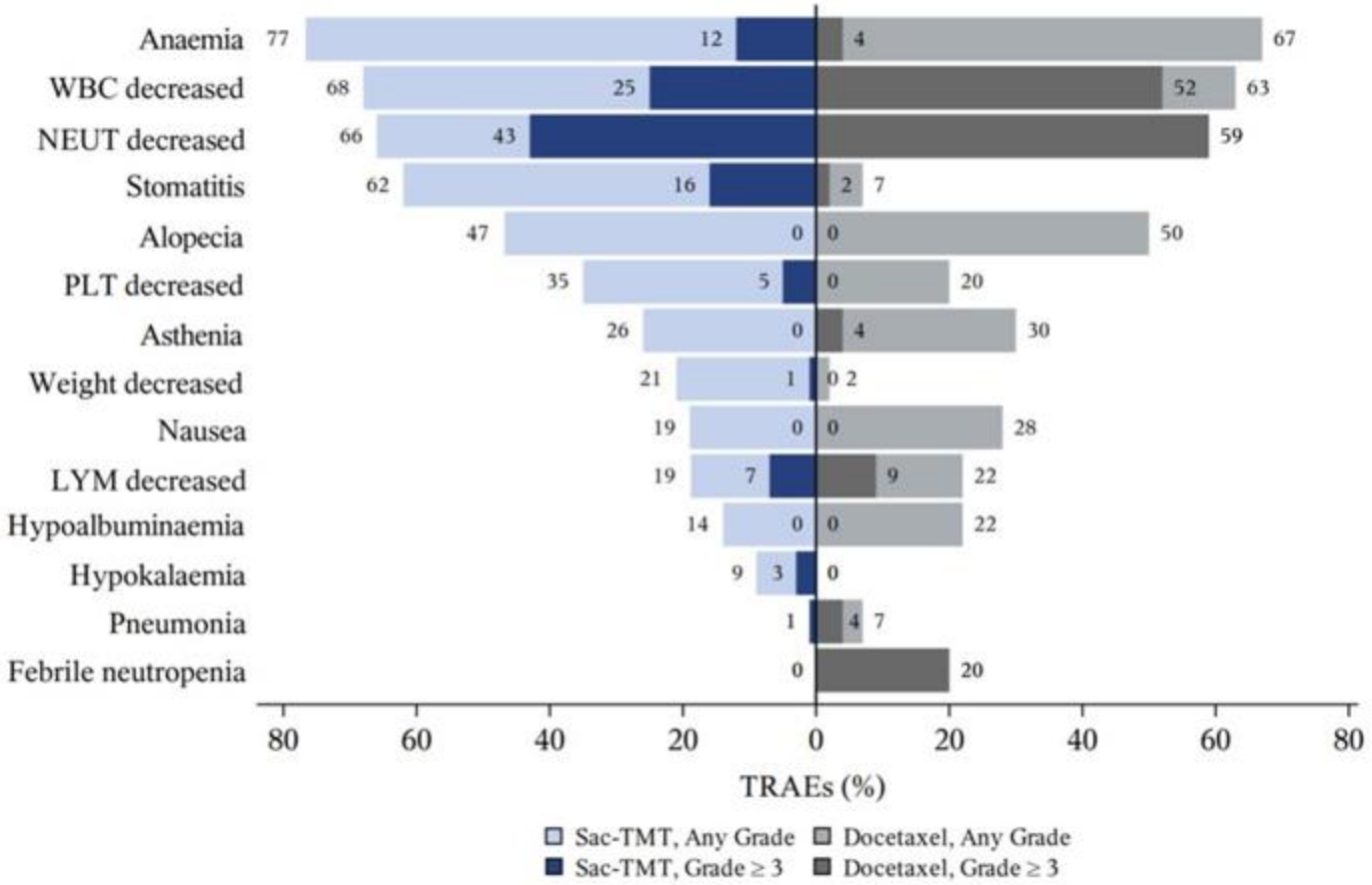
OPTITROP-LUNG03



- The most common TRAEs for both sac-TMT and docetaxel were hematologic toxicities.
  - No febrile neutropenia reported with sac-TMT.
- Ocular surface toxicity: blurred vision and ophthalmodynia occurred in 1 patient (1.1%, both grade 1) with sac-TMT.
- Interstitial lung disease (ILD): no cases of ILD were reported in sac-TMT group.

Zhang L. ASCO 2025

TROP2 ADCs

Study	Design	Patients	Results	Safety
Opti-TROP-Lung03	Phase II RCT of Sacituzumab tirumotecan (Sac-TMT) vs docetaxel	137 pts with mNSCLC with mEGFR, and PD on TKI and chemo (sequential or combination)	ORR=45.1% vs 15.6% mPFS=6.9 vs 2.8 (HR=0.3, P<0.001); 1-yr OS: 72.8% vs 54.2%; HR=0.49, P=0.007	Gr ≥ 3 TRAEs=56% vs 71.7%
TROPION-Lung05	Phase II study of Datopotamab deruxtecan (Dato-DXd)	137 pts with mNSCLC with AGA and PD on targeted therapy and plat-based chemo (56.9% had EGFRm)	ORR=43.6% (32.4-55.3) mPFS=5.8 months (5.4-8.3) mOS=13.6 months (9.9-NE) in the entire cohort	Gr ≥ 3 TRAEs = 28.5%
EVOKE-01	Phase III study of sacituzumab govitecan vs docetaxel	603 pts with mNSCLC with PD on platinum-based chemo, anti-PD(L)1 and targeted therapies (only 3.2% had EGFRm)	Negative trial mOS for SG-11.1 months vs docetaxel=9.8 months; HR, 0.84 (0.68-1.04), P=0.0534	Gr ≥ 3 TRAEs = 66.6% with SG, vs 75.7% with docetaxel
SKB264-II-08	Phase II study of sacituzumab govitecan	64 pts with EGFRm NSCLC	ORR=34% (23-47) mPFS=9.3 months (7.6-11.4); 1-yr OS=79%	Gr ≥ 3 TRAEs=71%

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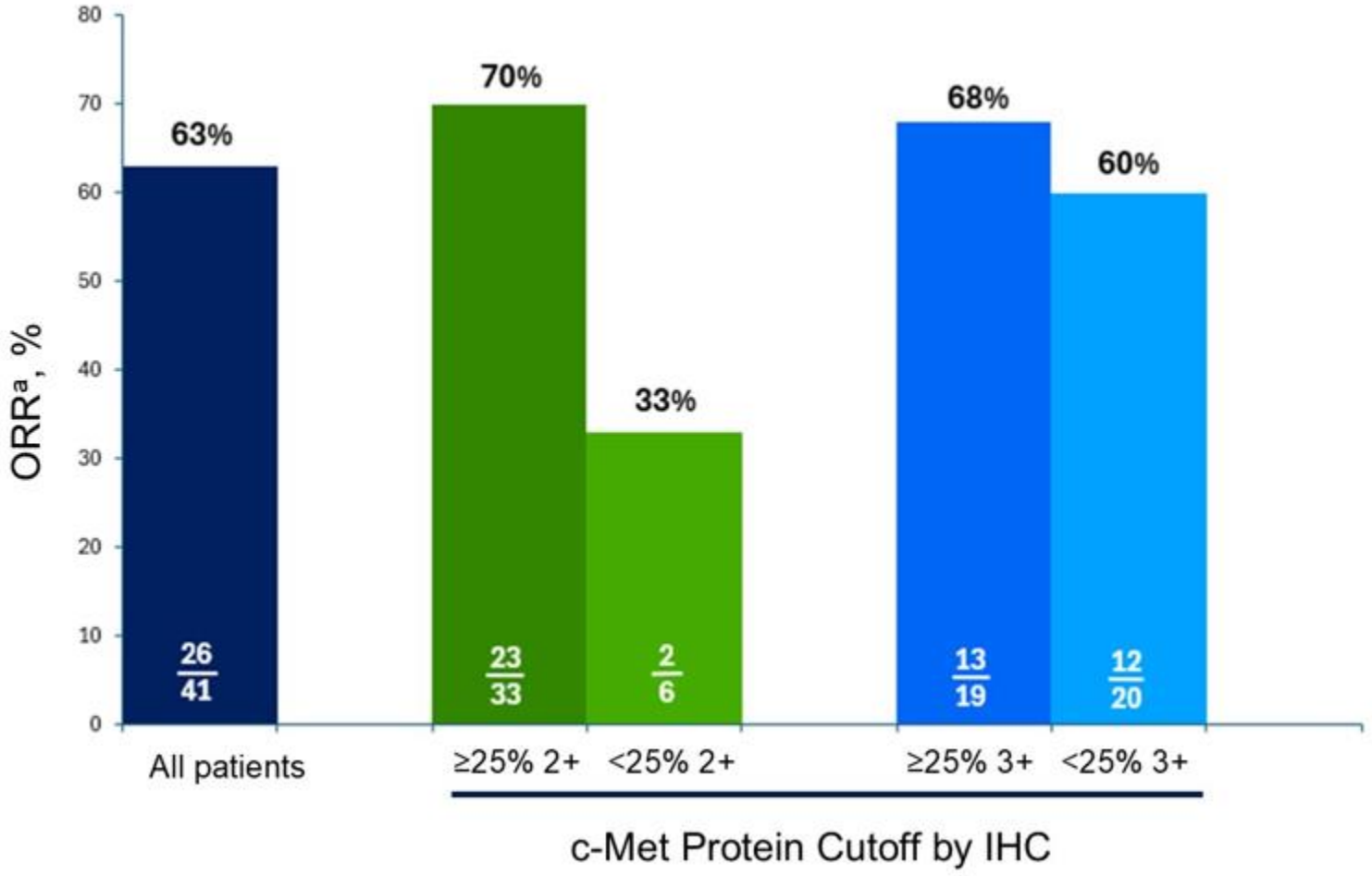
TELISOTUZUMAB ADIZUTECAN (3L+)



Camidge DR. ASCO 2025

EGFR exon 20

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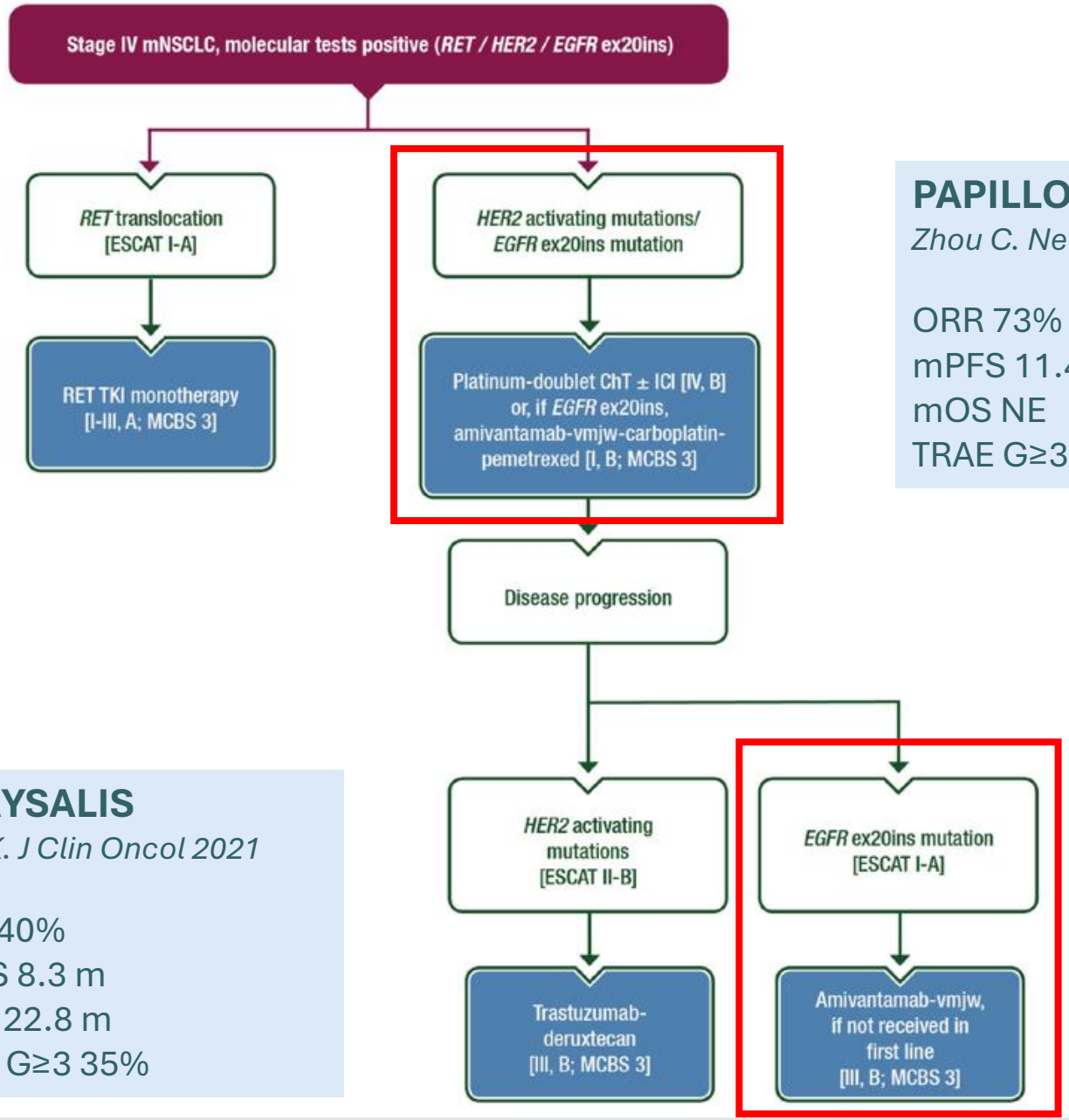
ESMO Oncogene-Addicted Metastatic Non-Small-Cell Lung Cancer Living Guideline
v1.2 January 2025



PAPILLON
Zhou C. New Engl J Med 2023

ORR 73%
mPFS 11.4 m
mOS NE
TRAE G≥3 ?

CHRYSALIS
Park K. J Clin Oncol 2021

ORR 40%
mPFS 8.3 m
mOS 22.8 m
TRAE G≥3 35%

REZILIENT1

Yu HA. ASCO 2025

REZILIENT1

Characteristic	Platinum-based chemotherapy without ex20ins-targeted therapy (n=143)	Prior ex20ins-targeted therapy (n=101)	Safety population (N=244)
Median number of prior systemic regimens, No. (range)	1 (0–6)	2 (1–7)	2 (0–7)
Prior chemotherapy, No. (%)	132 (92)	96 (95)	228 (93)
Prior anti–PD-(L)1, No. (%)	67 (47)	46 (46)	113 (46)
Prior targeted therapy, No. (%)	37 (26)	101 (100)	138 (57)
Amivantamab	0	84 (83)	84 (34)
Mobocertinib	0	40 (40)	40 (16)
Bevacizumab	14 (10)	16 (16)	30 (12)
Osimertinib	13 (9)	7 (7)	20 (8)
BLU-451	0	5 (5)	5 (2)
Cetuximab	4 (3)	0	4 (2)
Poziotinib	0	3 (3)	3 (1)
Sunvozertinib	0	3 (3)	3 (1)
Other[a]	17 (12)	9 (9)	26 (11)
Prior brain radiation, No. (%)	18 (13)	15 (15)	33 (14)
Brain metastasis untreated, No. (%)	30 (21)	40 (40)	70 (29)

Yu HA. ASCO 2025

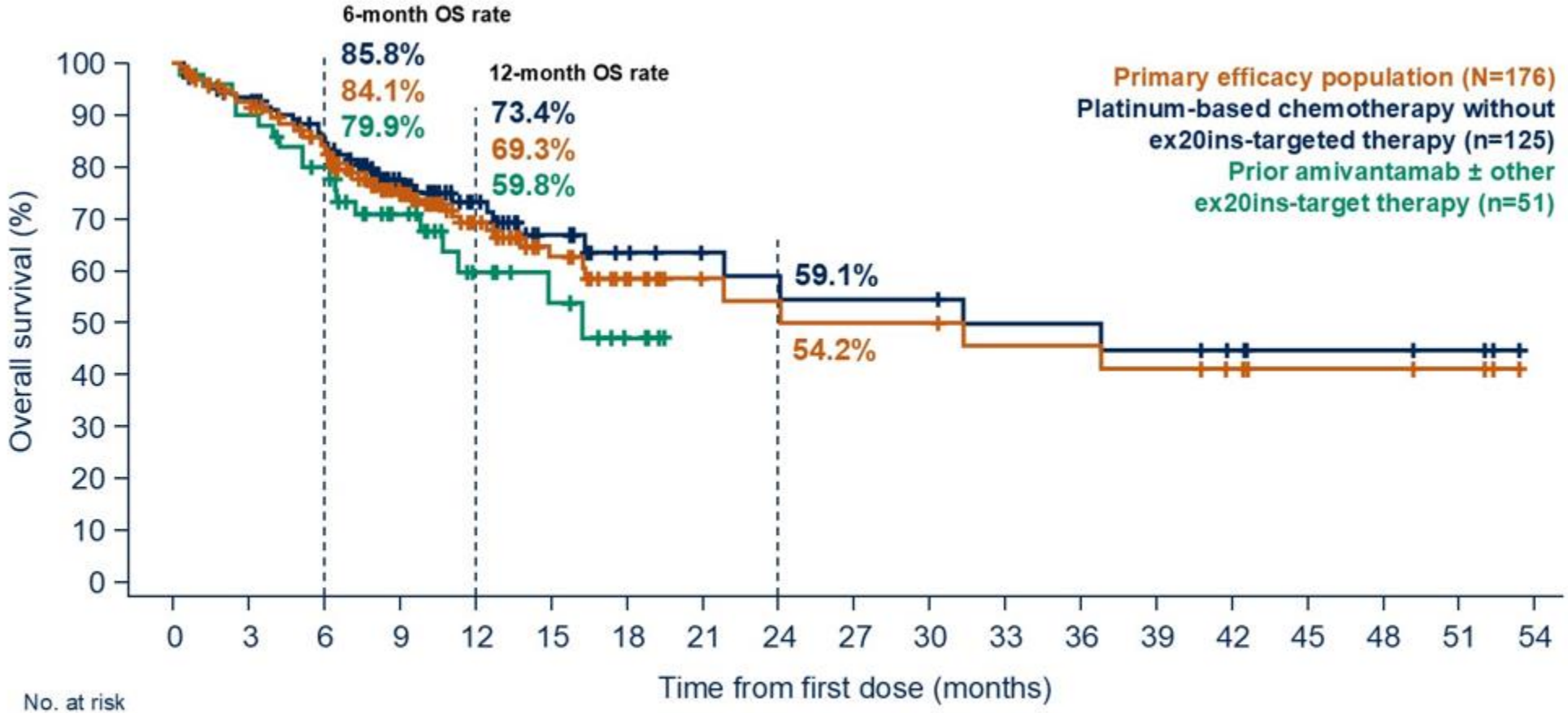
REZILIENT1

Efficacy per ICR in all patients and subgroups

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. (%)[b]			
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)

Yu HA. ASCO 2025

REZILIENT1



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

Yu HA. ASCO 2025

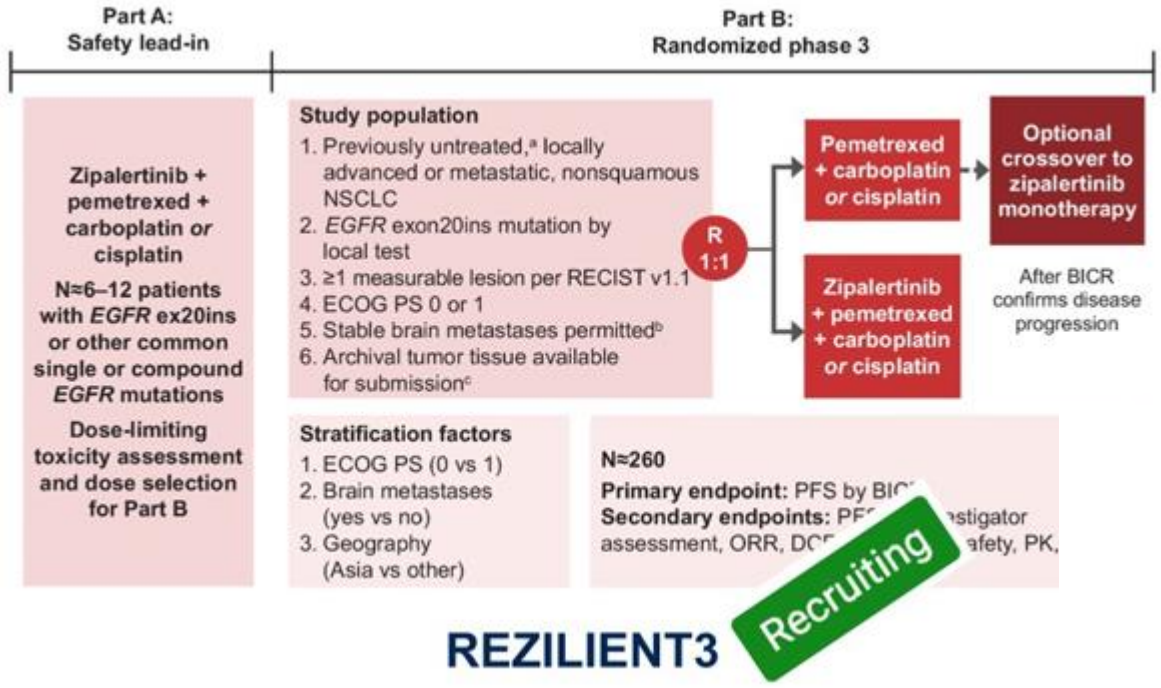
REZILIENT1

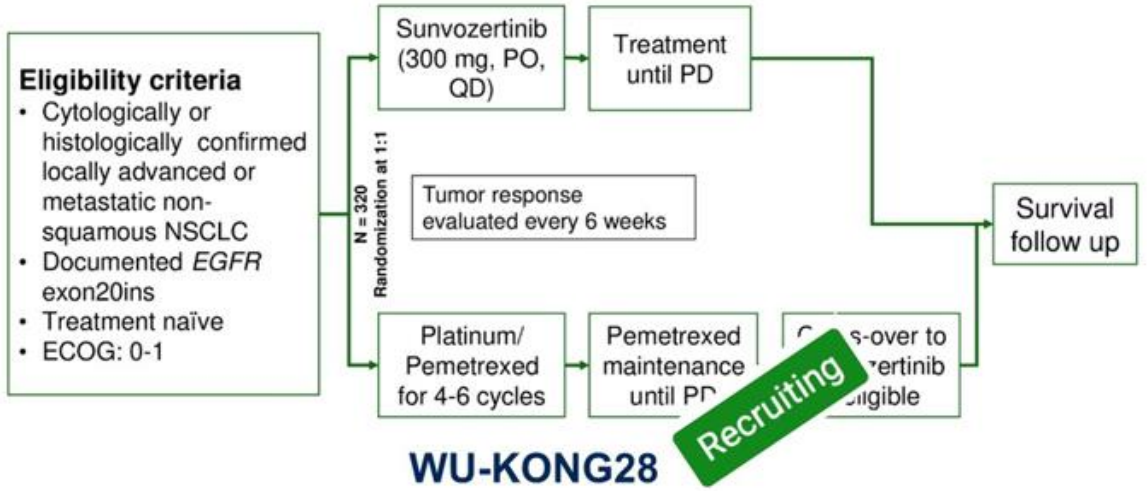
Any-grade TRAEs reported in ≥10% of patients, No. (%)	Any grade	Grade 3
Paronychia	94 (38.5)	0
Rash	74 (30.3)	6 (2.5)
Dermatitis acneiform	60 (24.6)	1 (0.4)
Dry skin	60 (24.6)	0
Diarrhea	53 (21.7)	5 (2.0)
Stomatitis	49 (20.1)	4 (1.6)
Anemia	48 (19.7)	17 (7.0)
Pruritus	44 (18.0)	1 (0.4)
Nausea	35 (14.3)	2 (0.8)
Rash maculopapular	34 (13.9)	3 (1.2)
Fatigue	29 (11.9)	0

- Anemia was the most common grade 3 TRAE
- Other grade ≥3 TRAEs reported in ≥5 patients included pneumonitis and rash (6 patients [2.5%] each), and alanine aminotransferase increased, diarrhea, and platelet count decreased (5 patients [2.0%] each)
- Twelve patients (4.9%) had treatment-related pneumonitis, 5 of whom had received prior immunotherapy
  - Grade 1, n=3; grade 2, n=3; grade 3, n=5; grade 5, n=1

Yu HA. ASCO 2025

FUTURE PERSPECTIVES





Corassa M. ASCO 2025

KRAS G12C

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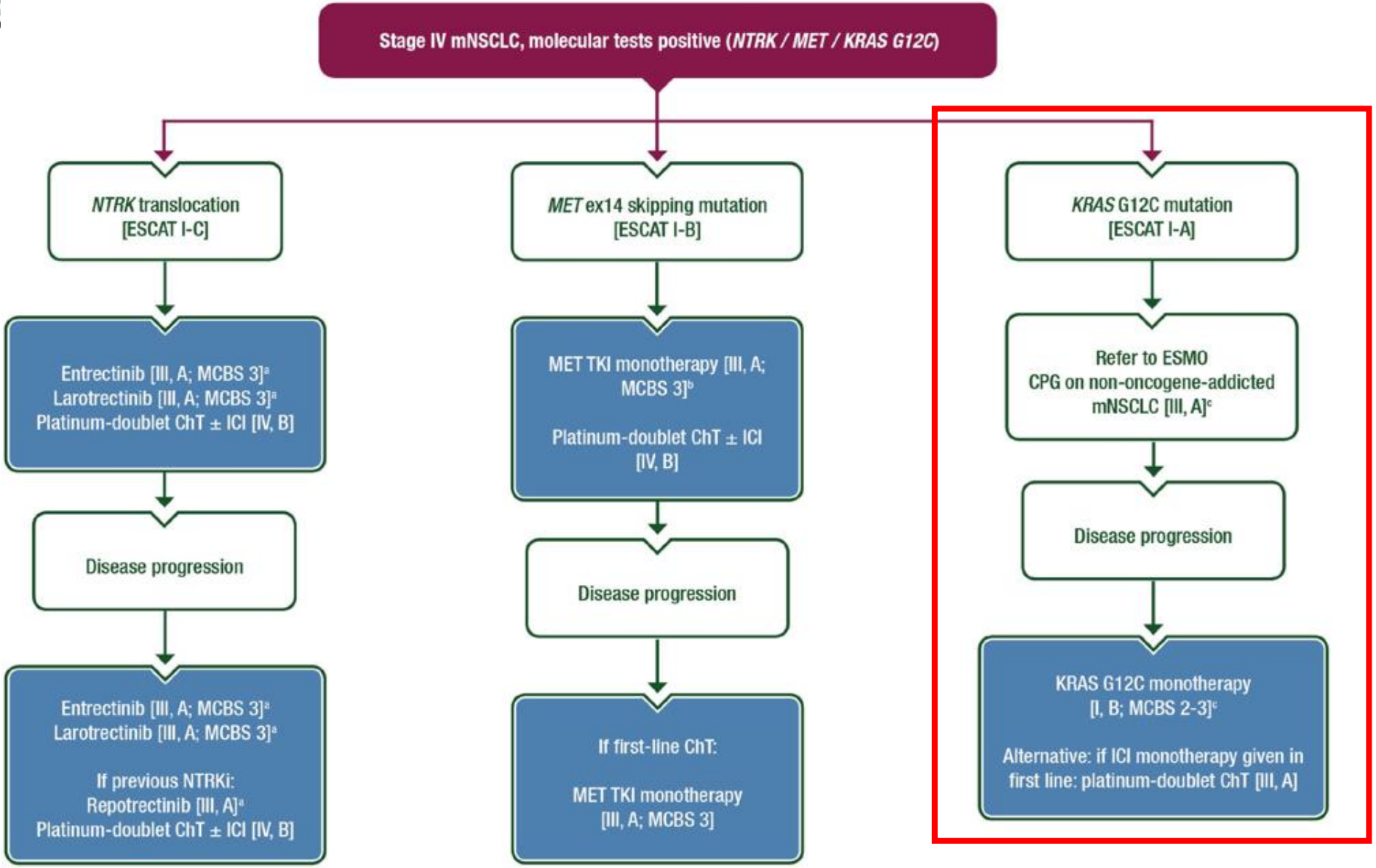
v1.2 January 2025



LUNG-MAP S1900E

G12C is the most common *KRAS* variant – 13% of NSCLC

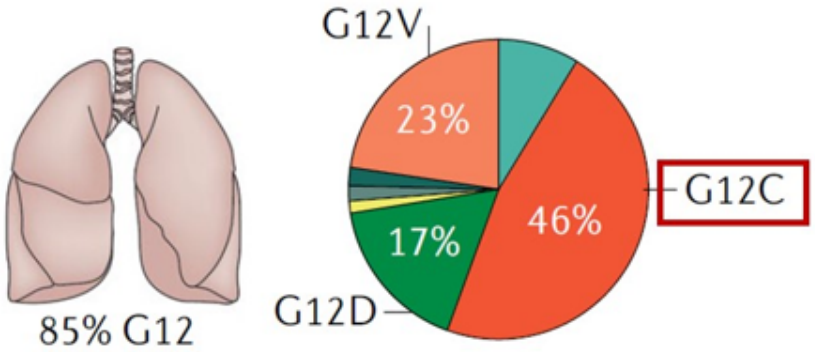


Figure from Moore AR et al Nat Rev Drug Discov 2020[1]

KRAS G12C NSCLC has frequent co-mutations in tumor suppressor genes

Co-MUT	Prevalence in *KRAS* G12C NSCLC
TP53	18-50%
STK11	10-28%
KEAP1	6-23%

Real world registry data summarized in Lim TKH et al Lung Cancer 2023[3]

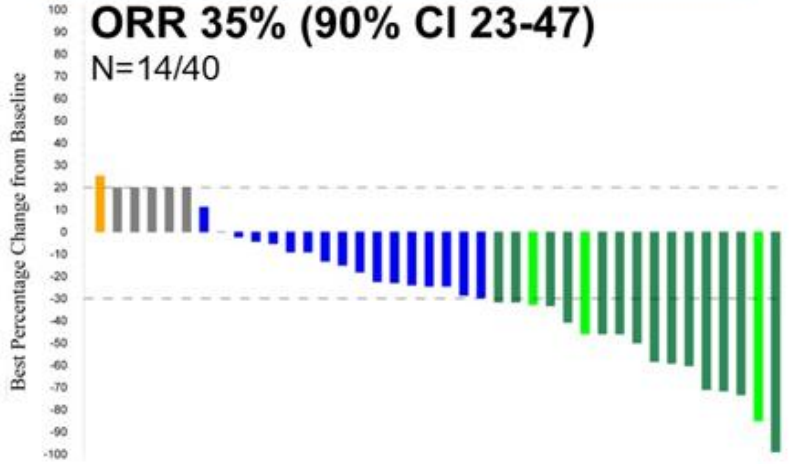
The presence of specific co-mutations may influence the clinical activity of approved KRAS G12C inhibitors (sotorasib, adagrasib)[4,5,9,10]

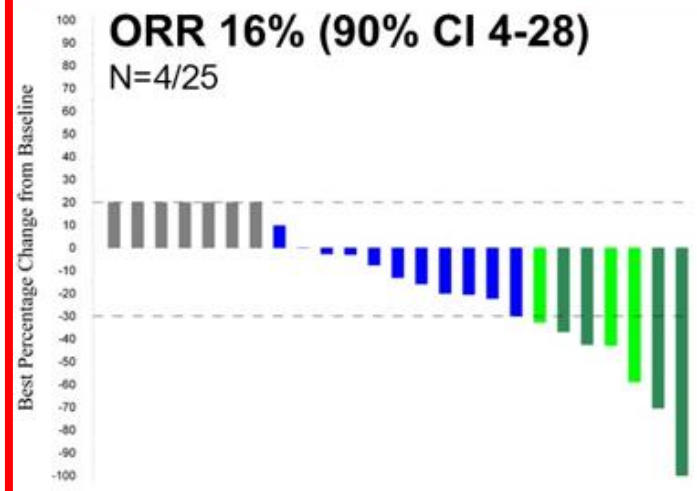
LungMap S1900E examines the impact of co-mutations on sotorasib in *KRAS* G12C NSCLC in a prospective trial

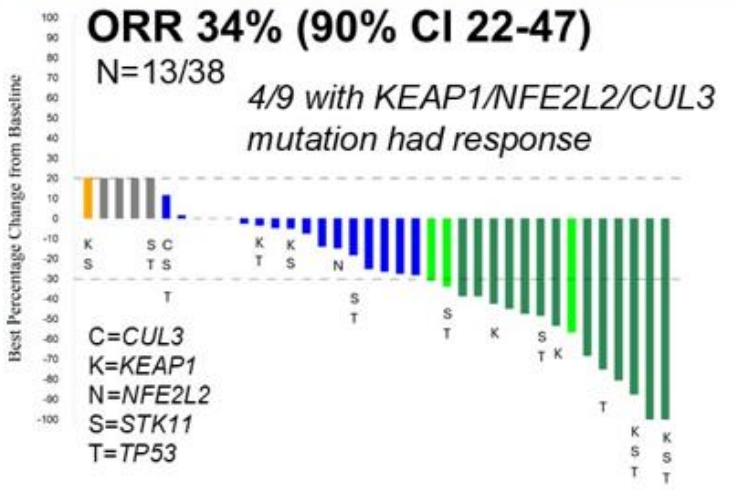
Padda SK. ASCO 2025

LUNG-MAP S1900E

	TP53 CO-MUT	*STK11* CO-MUT	OTHER CO-MUT
	ORR 35% (90% CI 23-47) N=14/40	**ORR 16% (90% CI 4-28)** N=4/25	**ORR 34% (90% CI 22-47)** N=13/38 *4/9 with KEAP1/NFE2L2/CUL3 mutation had response*
Median PFS (95% CI)	**5.7** mo (3.0-8.4)	**4.1** mo (2.6-7.1)	**7.1** mo (5.5-8.5)
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%







Padda SK. ASCO 2025

KRYSTAL-7

Key eligibility criteria

- Advanced, unresectable or metastatic NSCLC with *KRAS*^{G12C} mutation[b]
- No prior systemic therapy for locally advanced/metastatic disease[c]
- Known PD-L1 TPS (local or central testing)[d]
- Treated, neurologically stable brain metastases allowed

ADA 400 mg PO BID +
PEMBRO 200 mg IV Q3W[e,f]

Primary endpoint

- ORR per investigator assessment (RECIST v1.1)

Secondary endpoints

- DOR and PFS per investigator assessment
- OS
- Safety

Jänne PA. ASCO 2025

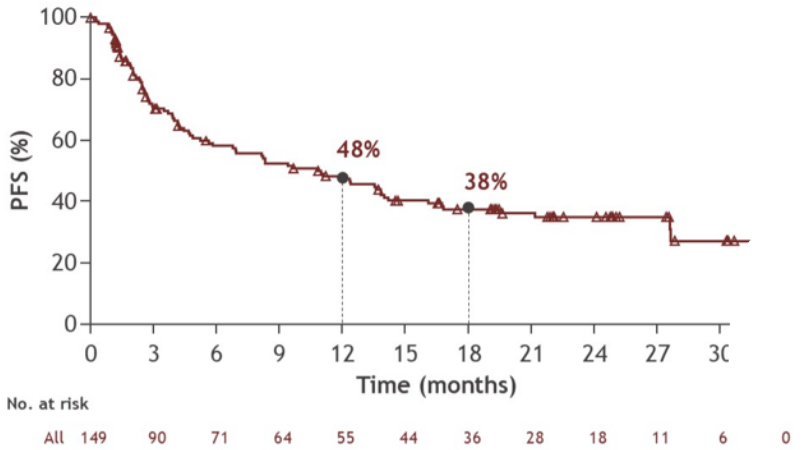
KRYSTAL-7

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)
Blood ALP increase	29 (19)	12 (8)	7 (5)	10 (7)	0
GGT increase	10 (7)	2 (1)	2 (1)	6 (4)	0
Blood bilirubin increase	6 (4)	4 (3)	1 (< 1)	1 (< 1)	0
Abnormal hepatic function	6 (4)	3 (2)	1 (< 1)	2 (1)	0
Hepatitis	6 (4)	0 (0)	3 (2)	3 (2)	0
	All patients (N = 149)				
Hepatic TRAEs leading to					
ADA discontinuation only	2 (1)[c]				
PEMBRO discontinuation only	9 (6)[d]				
ADA and PEMBRO discontinuation	1 (< 1)[e]				

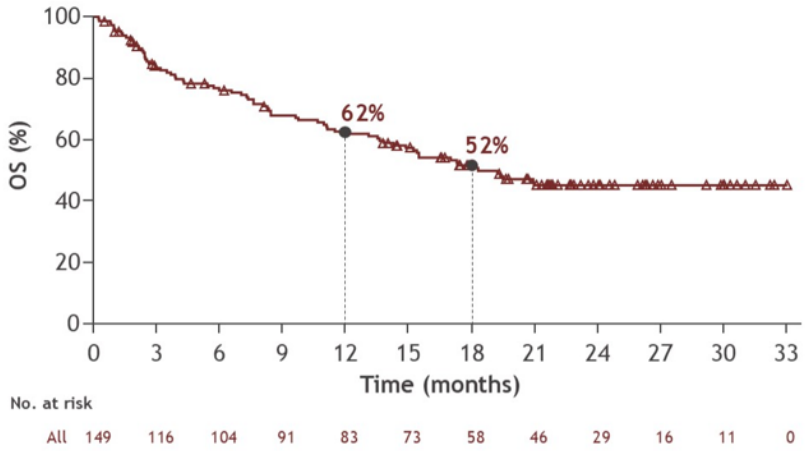
Jänne PA. ASCO 2025

KRYSTAL-7

	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



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

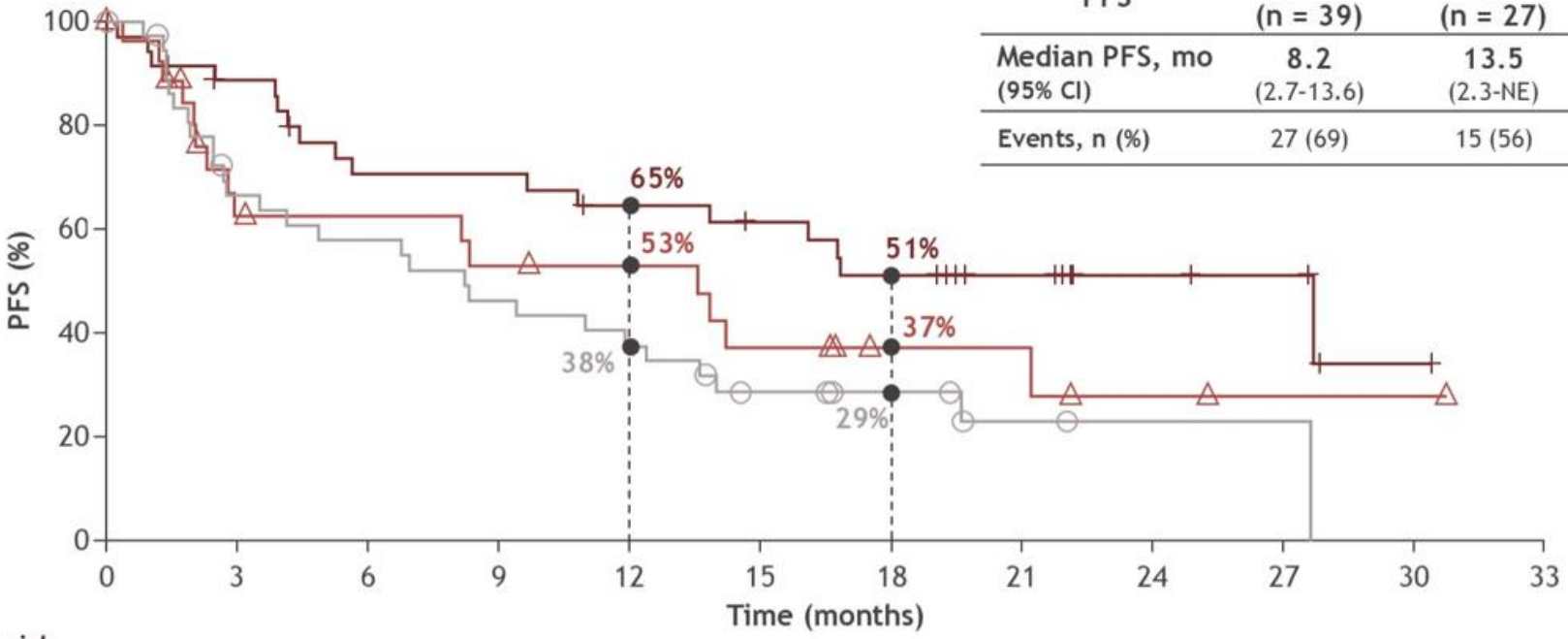


OS	All patients (N = 149)
Median OS, mo (95% CI)	18.3 (14.3-NE)
Events, n (%)	73 (49)

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)

Jänne PA. ASCO 2025

KRYSTAL-7



PFS	PD-L1 < 1% (n = 39)	PD-L1 1-49% (n = 27)	PD-L1 ≥ 50% (n = 38)[b]
Median PFS, mo (95% CI)	8.2 (2.7-13.6)	13.5 (2.3-NE)	27.7 (9.6-NE)
Events, n (%)	27 (69)	15 (56)	17 (45)

No. at risk												
PD-L1 < 1%	39	23	20	16	13	8	6	3	1	1	0	0
PD-L1 1-49%	27	14	13	11	10	7	4	4	2	1	1	0
PD-L1 ≥ 50%	38	30	23	23	20	18	15	11	6	4	1	0

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

[a]PFS per investigator assessment in the biomarker-evaluable population. 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]Patients with PD-L1 TPS ≥ 50% included 18 patients with PD-L1 TPS 50-79% and 20 patients with PD-L1 TPS ≥ 80%.

Jänne PA. ASCO 2025

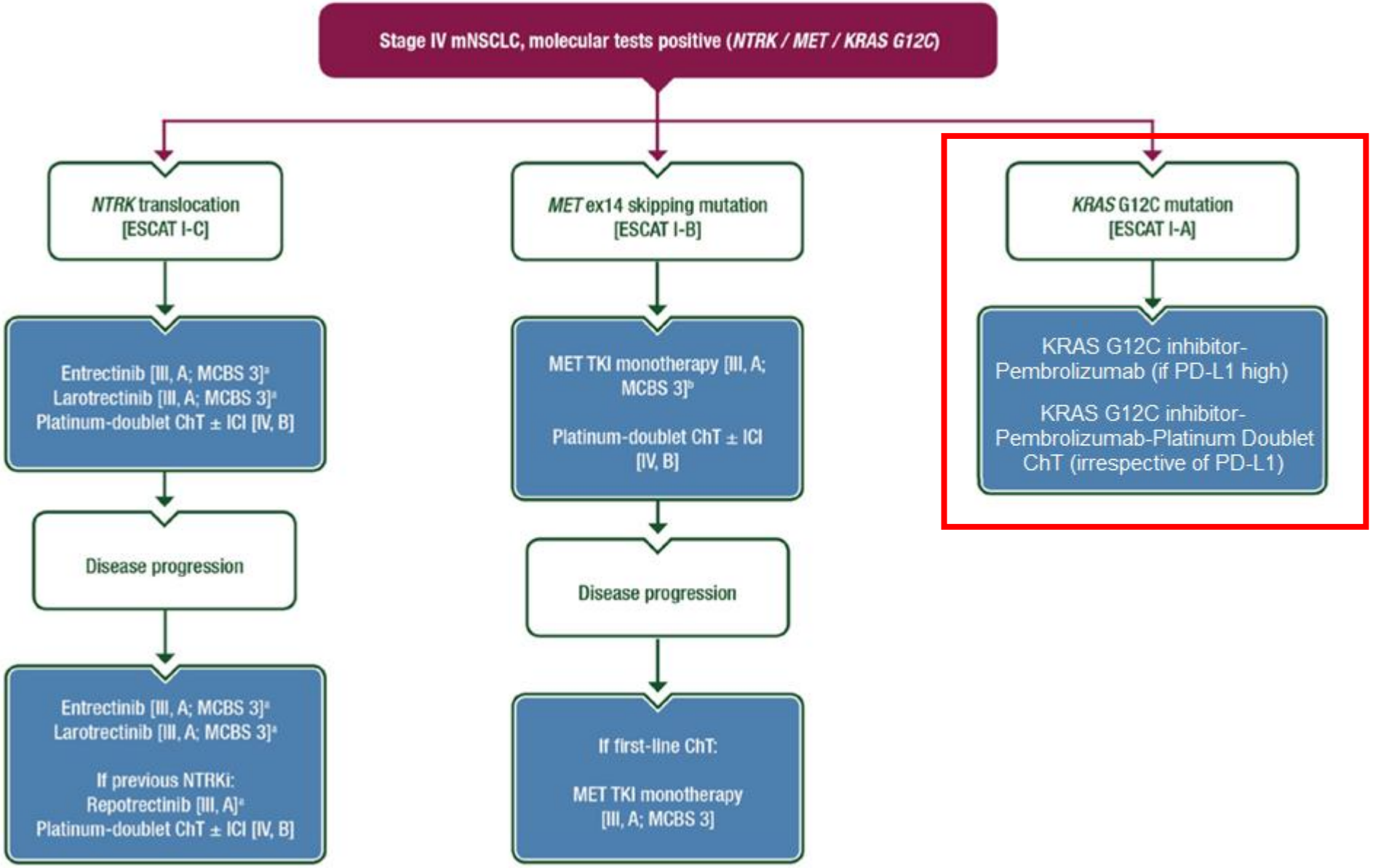
FUTURE PERSPECTIVES

Clinical Trial Name	Phase	Treatment	Status
KRYSTAL-4	3	ADA Plus Pembro Plus Chemo vs. Placebo Plus Pembro Plus Chemo	Recruiting
KRYSTAL-7	3 portion	ADA + Pembro in PD-L1 ≥ 50%	Recruiting
SUNRAY-01	3	Olomorasib and Pembrolizumab With or Without Chemotherapy	Recruiting
MK-1084-004	3	MK-1084 Plus Pembro vs. Placebo Plus Pembro in PD-L1 ≥ 50%	Recruiting
Krascendo 2	3	Divarasib Plus Pembro vs. Pembro Plus Chemo	Not yet recruiting
CodeBreaK-202	3	Sotorasib Plus Chemo vs. Pembrolizumab Plus Chemo in PD-L1 negative	Recruiting

Leal T. ASCO 2025

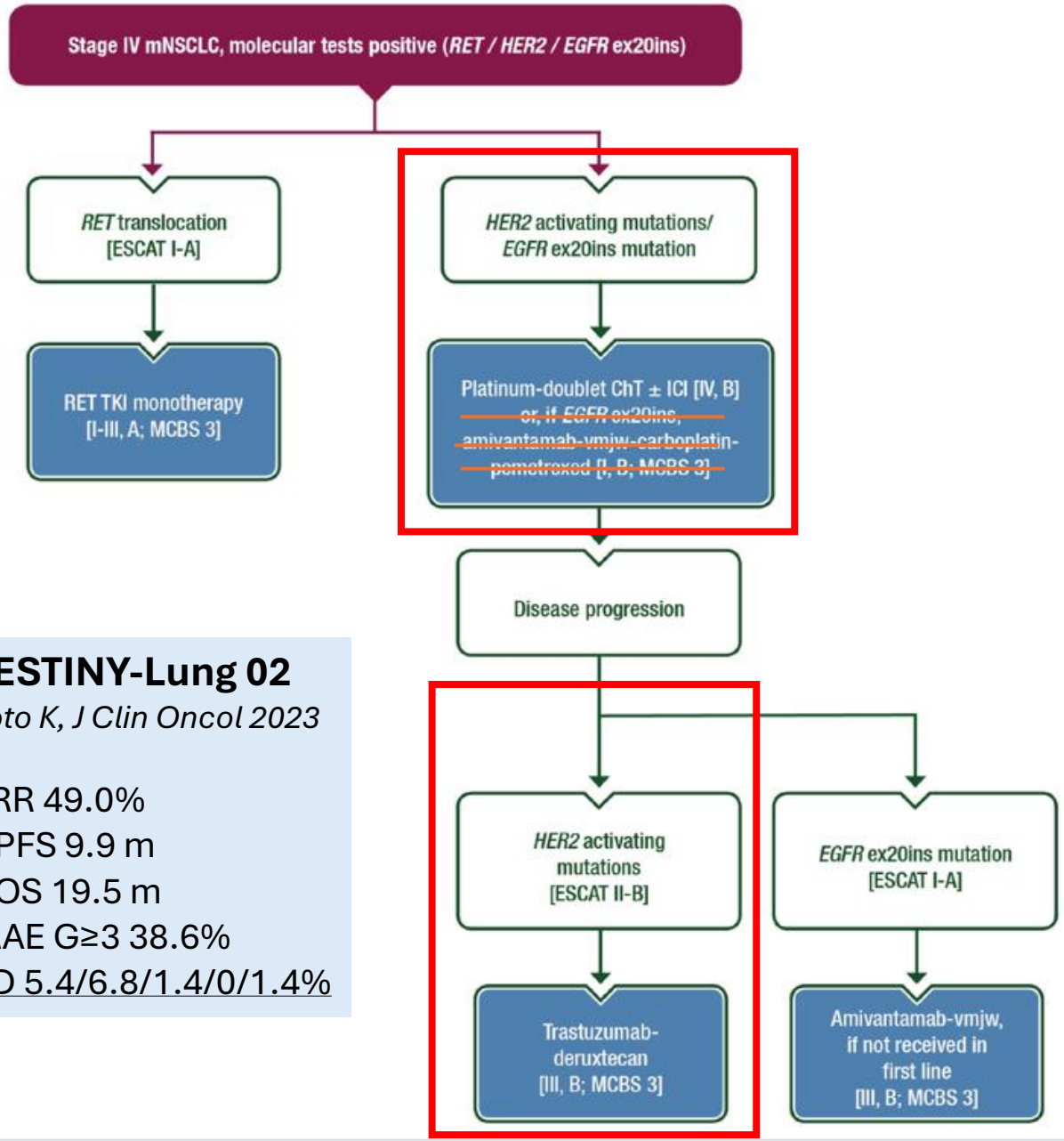
CLINICAL PRACTICE GUIDELINES

ESMO Oncogene-Addicted Metastatic Nor
Lung Cancer Living Guideline
v1.2 January 2025



(hypothetically)

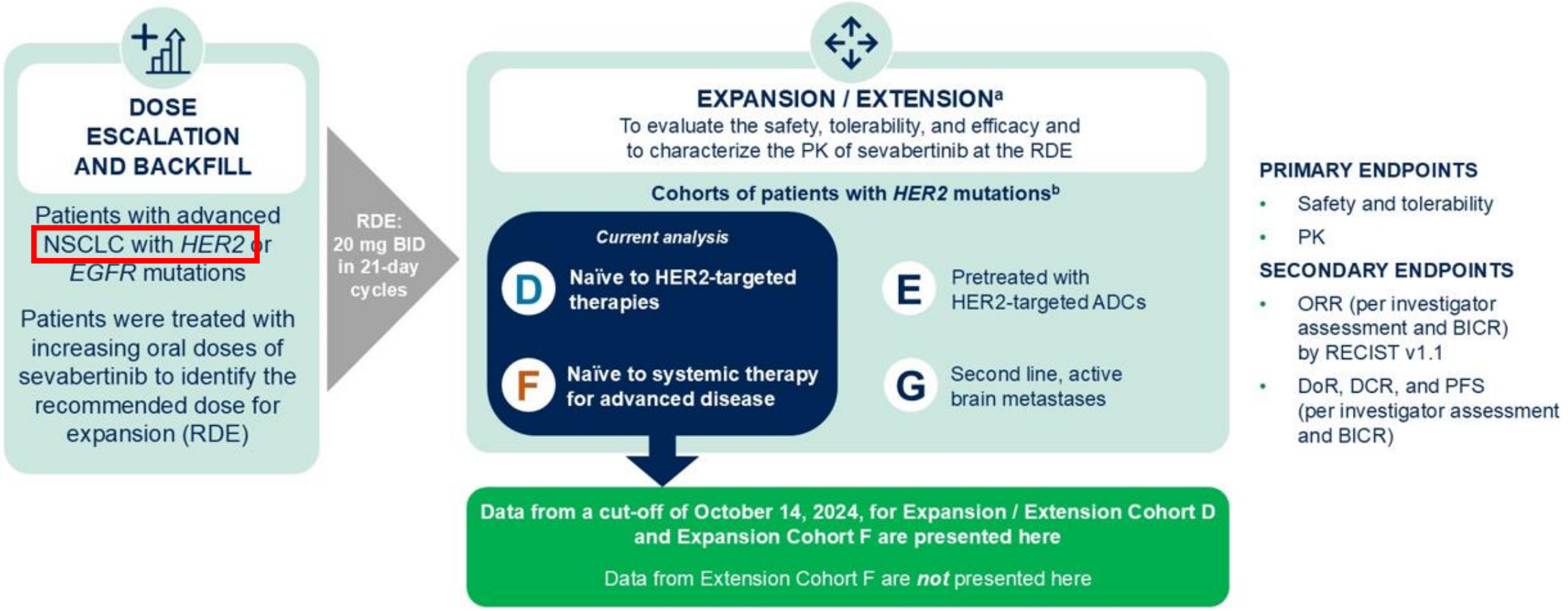
HER2



DESTINY-Lung 02
Goto K, J Clin Oncol 2023

ORR 49.0%
mPFS 9.9 m
mOS 19.5 m
TRAE G≥3 38.6%
ILD 5.4/6.8/1.4/0/1.4%

SOHO-01



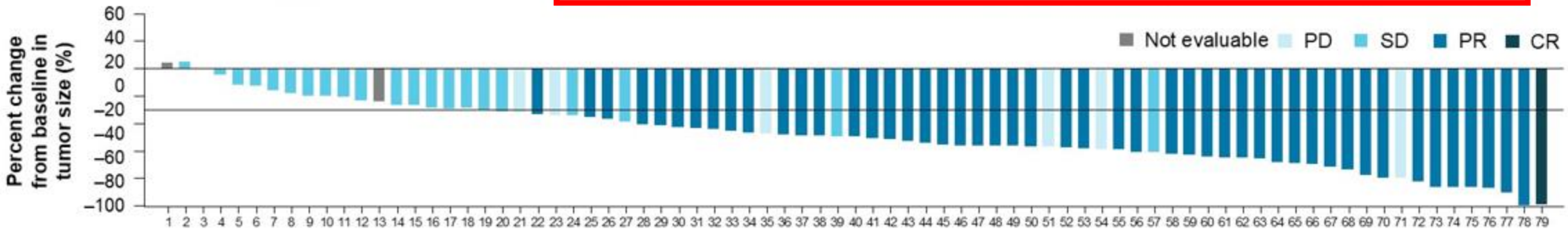
Loong HH. ASCO 2025

SOHO-01

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]



Number of prior systemic anti-cancer therapies, *n* (%)	
0	0
1	46 (56.8)
2	16 (19.8)
≥3	19 (23.5)

Patients with brain metastases at baseline (ORR 64.7%)

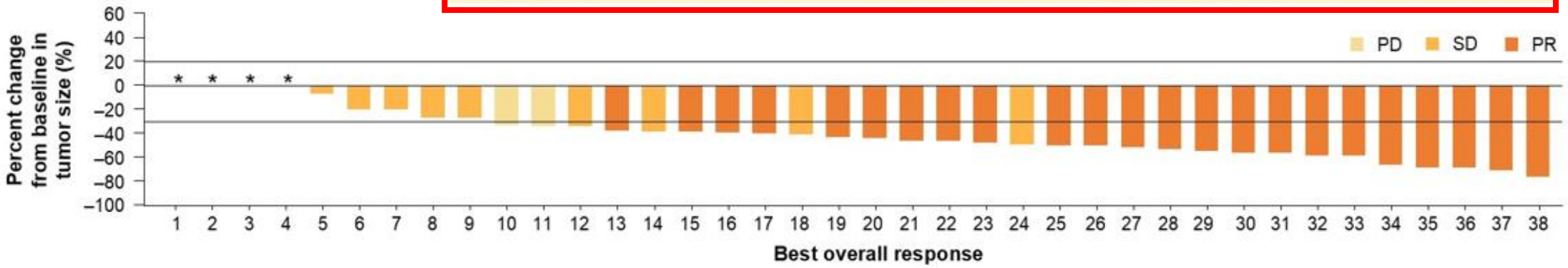
Loong HH. ASCO 2025

SOHO-01

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

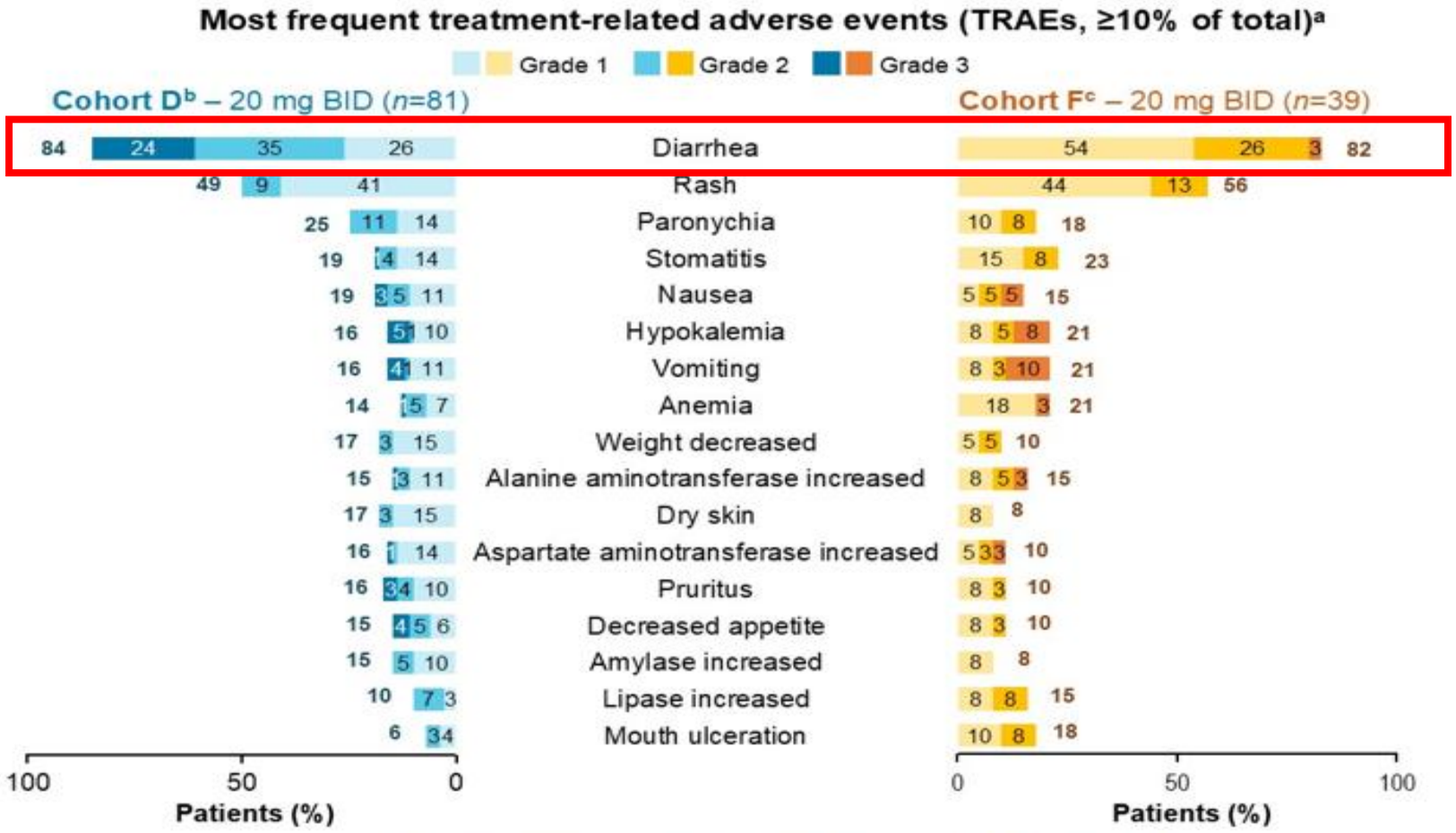
Median follow-up: 5.6 months[a]

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]



Loong HH. ASCO 2025

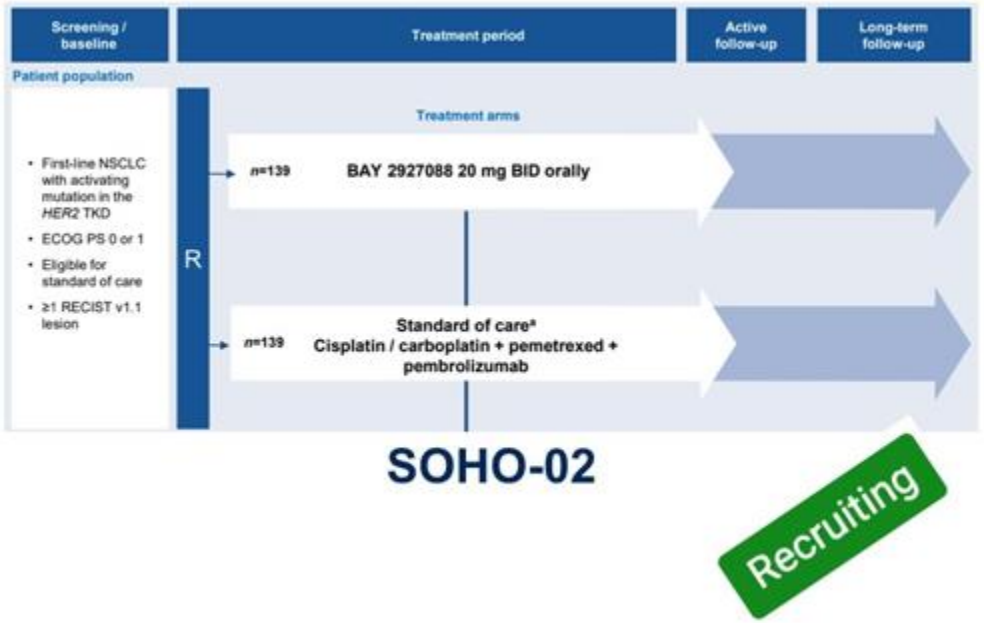
SOHO-01



There were no reported cases of interstitial lung disease or pneumonitis

Loong HH. ASCO 2025

FUTURE PERSPECTIVES



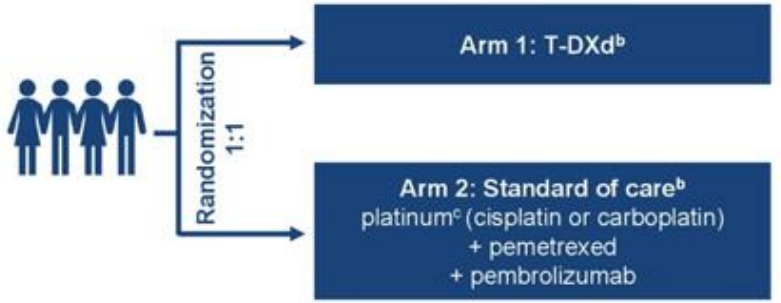
SOHO-02

Recruiting

Patient population (N≈264)

- Unresectable, locally advanced (not amenable to curative therapy), or metastatic nonsquamous NSCLC with *HER2* exon 19 or 20 mutations[a]
- Naive to systemic therapy in the locally advanced or metastatic setting
- No known other targetable oncogenic mutations/alterations

[a] *HER2* mutations may be detected in tissue or ctDNA.
[b] Crossover is not permitted.
[c] Investigator's choice of cisplatin or carboplatin.



DESTINY-Lung04

Recruiting

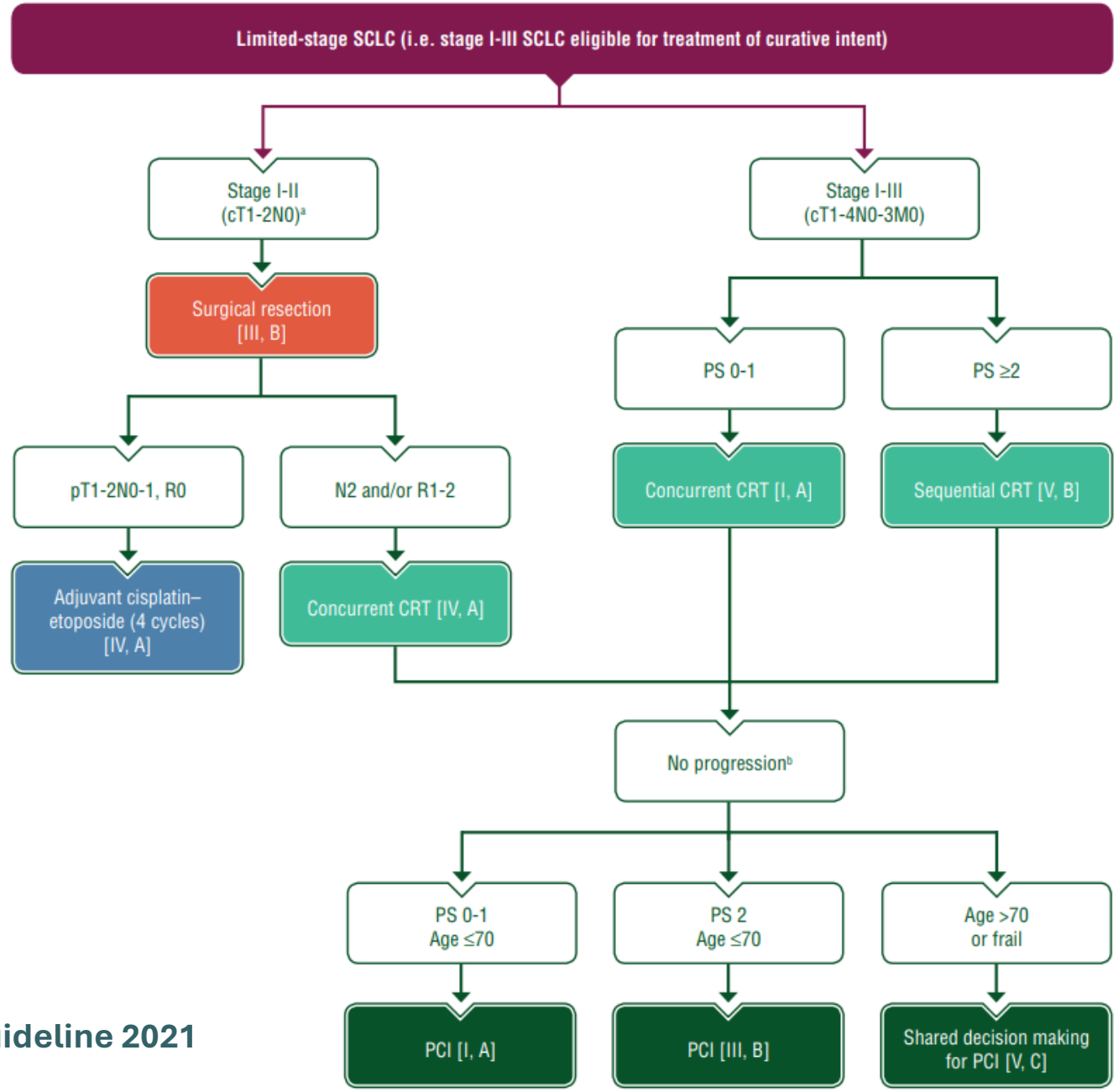
Beamion-Lung 02

Recruiting

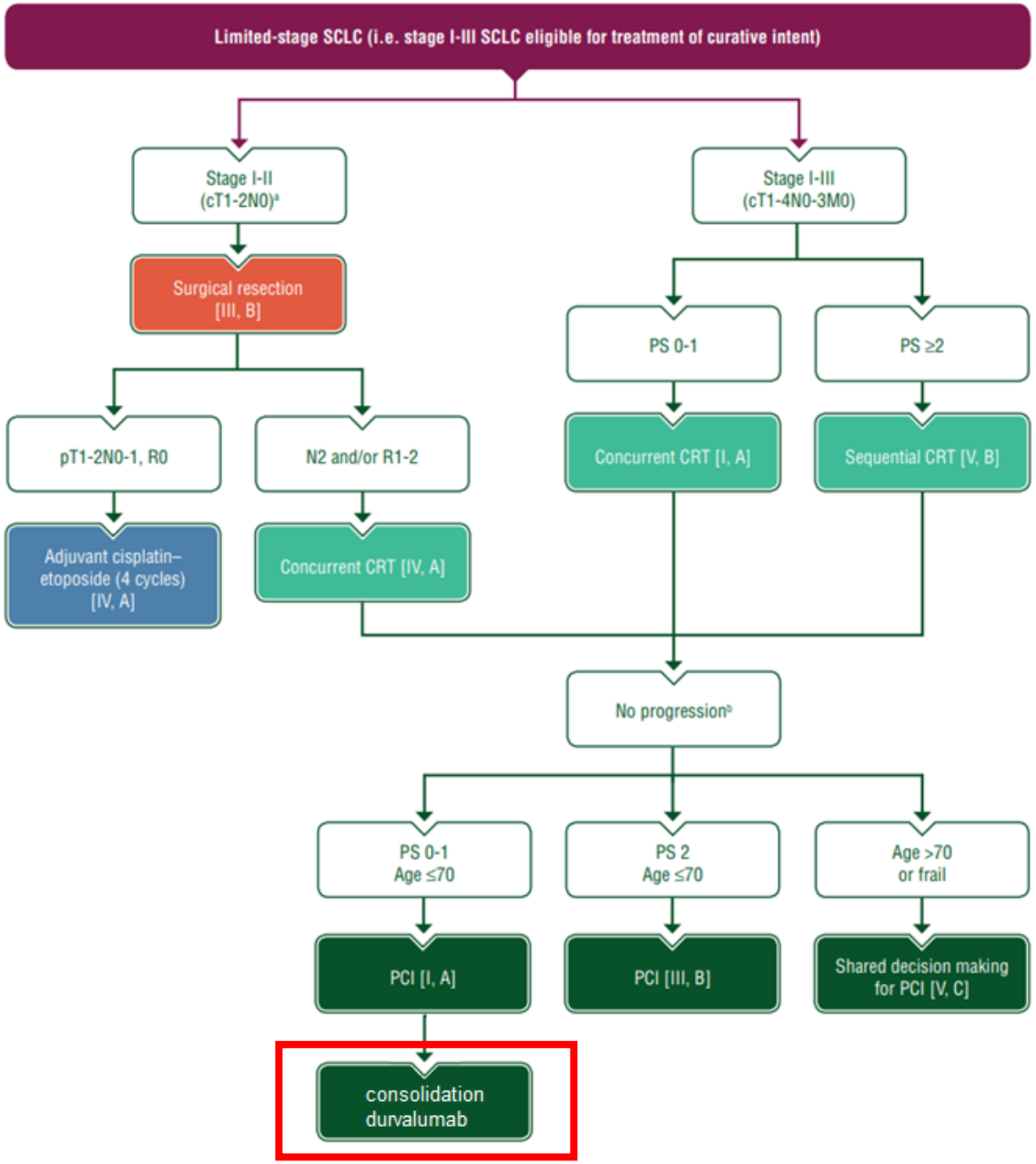
Corassa M. ASCO 2025

SMALL CELL LUNG CANCER

PRESENTED BY: Jo Raskin MD

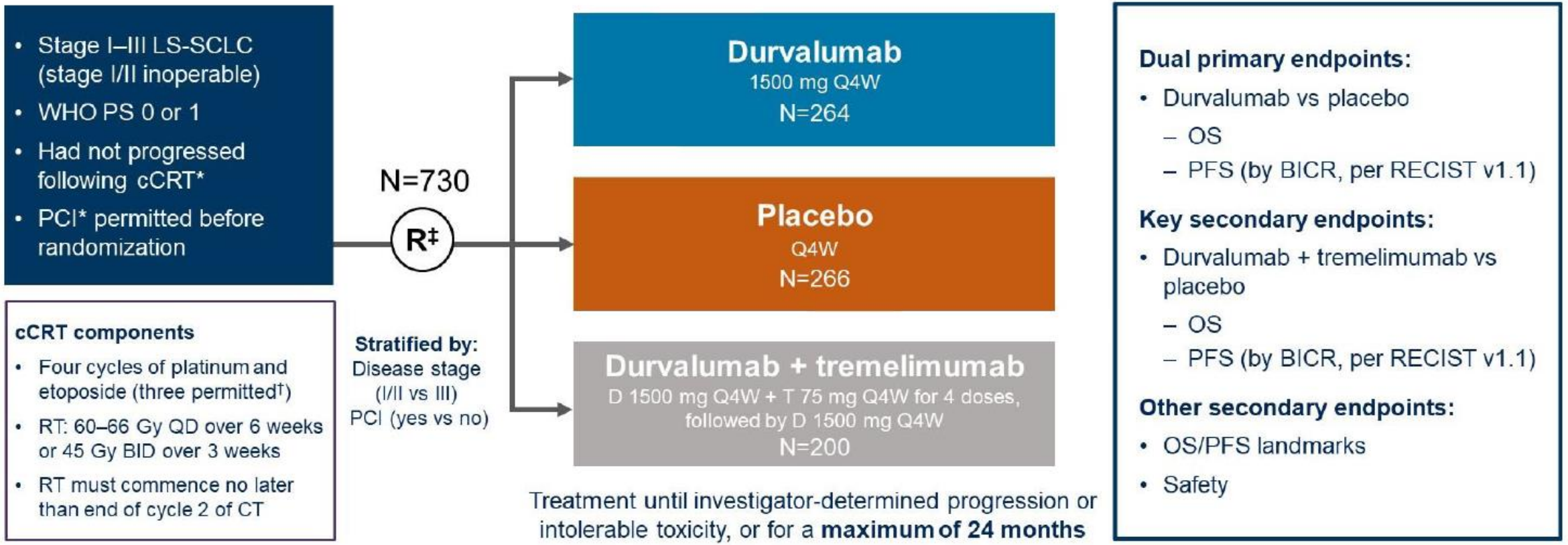


ESMO Clinical Practice Guideline 2021
(Dingemans A.C. Ann Oncol 2021)



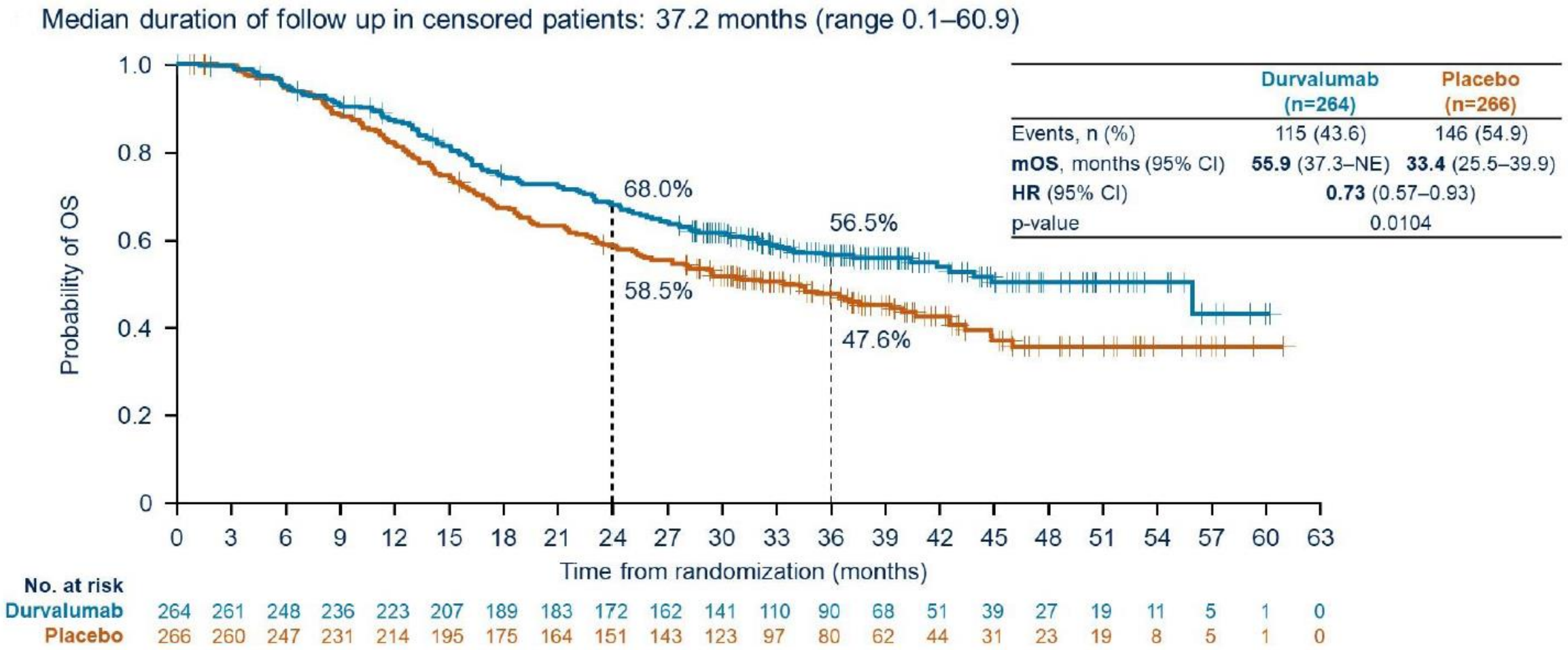
ESMO Clinical Practice Guideline 2025
(hypothetically)

ADRIATIC



Spigel DR. ASCO 2024

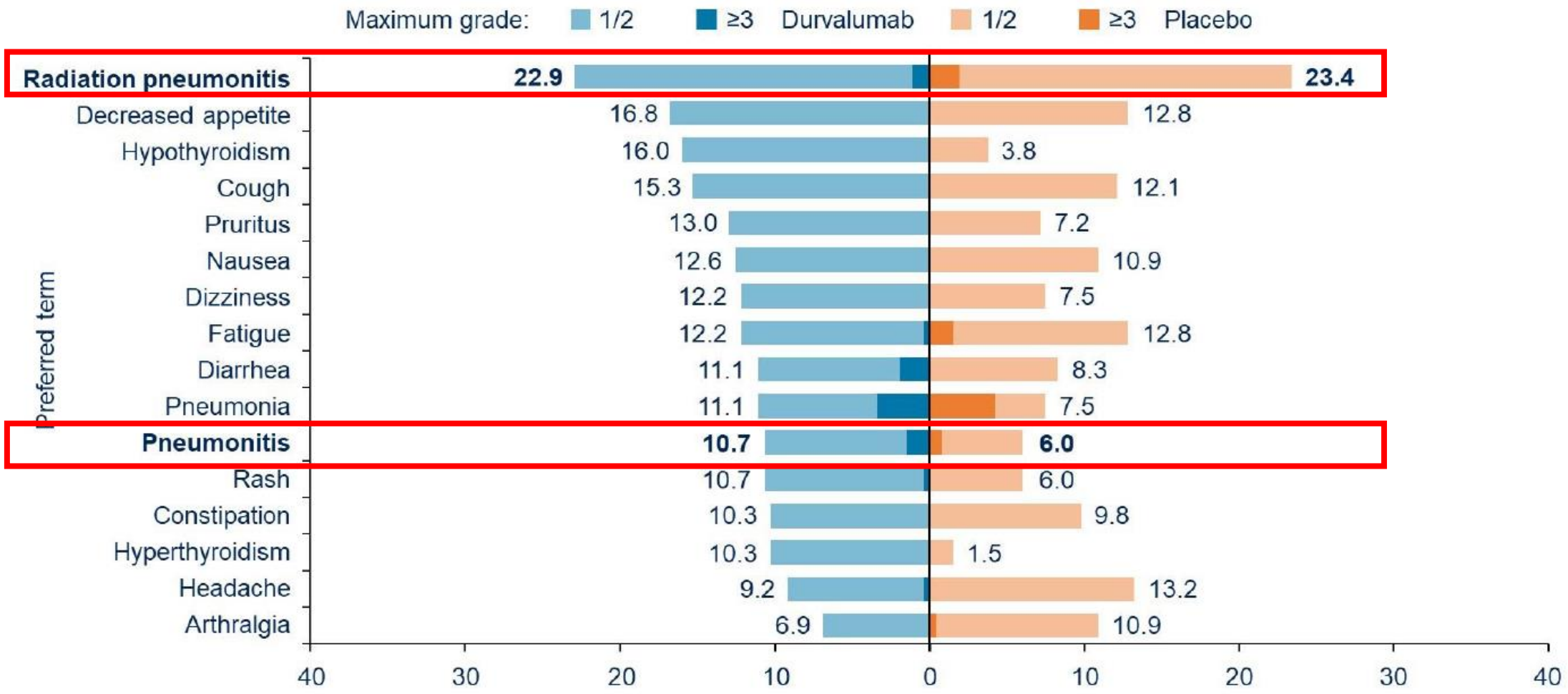
ADRIATIC



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

Spigel DR. ASCO 2024

ADRIATIC



Spigel DR. ASCO 2024

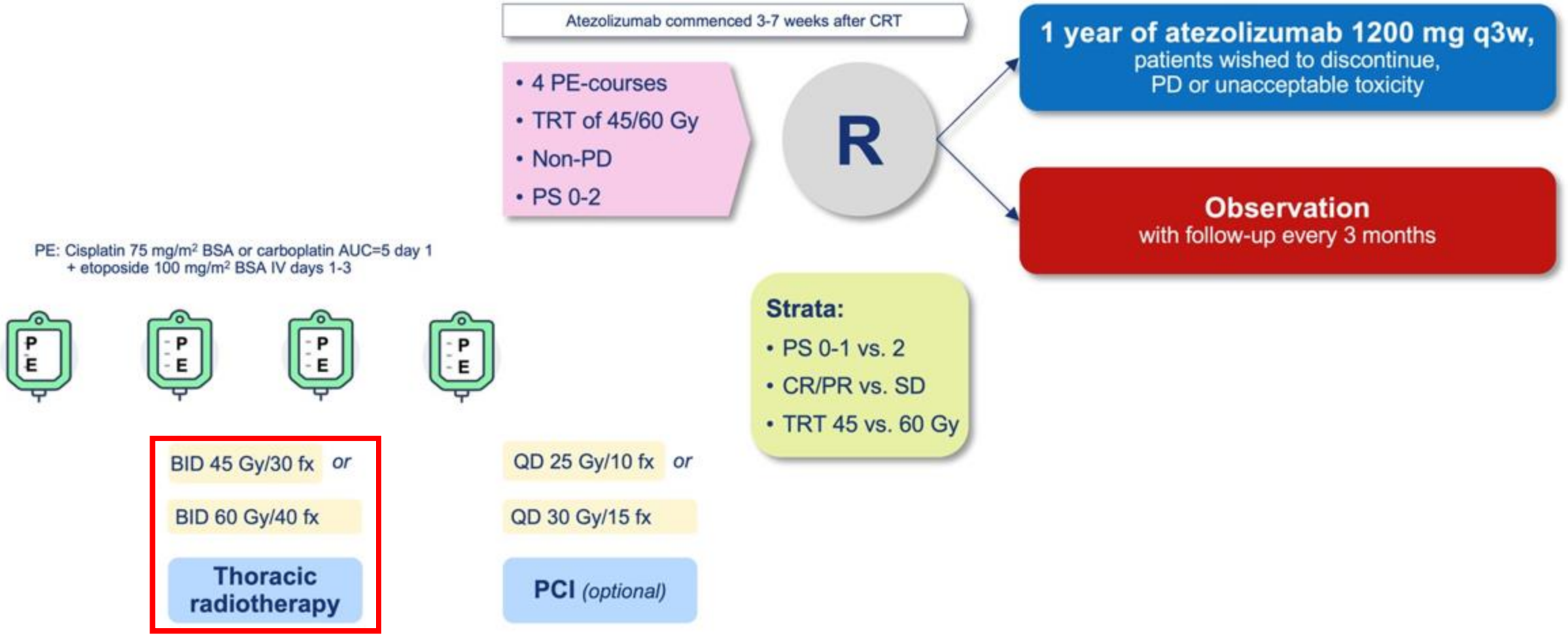
ADRIATIC

Higher proportions of stage I/II disease, prior BID radiotherapy and prior PCI were seen in LTPs vs EPs in both arms; there was a higher proportion of patients with WHO PS 0 in LTPs vs EPs in the durvalumab arm

	Durvalumab (n=264)		Placebo (n=266)	
	EP	LTP	EP	LTP
n (% of ITT population)	83 (31.4)	113 (42.8)	97 (36.5)	100 (37.6)
Median age, years (range)	61.0 (36–77)	63.0 (28–84)	61.0 (39–79)	63.0 (28–79)
Sex, %				
Male / female	67.5 / 32.5	61.1 / 38.9	74.2 / 25.8	72.0 / 28.0
Race, %				
White / Asian	48.2 / 50.6	50.4 / 48.7	58.8 / 38.1	48.0 / 52.0
WHO PS, %				
0	43.4	54.9	49.5	45.0
1	56.6	45.1	50.5	55.0
Disease stage, %				
I or II	6.0	17.7	7.2	19.0
III	94.0	82.3	92.8	81.0
Smoking history, %				
Current or former / never smoker	90.4 / 9.6	89.4 / 10.6	91.8 / 8.2	89.0 / 11.0
Prior platinum agent, %				
Carboplatin / cisplatin	30.1 / 69.9	38.1 / 61.9	35.1 / 64.9	32.0 / 68.0
Prior radiotherapy, %				
BID	20.5	31.9	24.7	35.0
QD	79.5	68.1	75.3	65.0
Response to prior cCRT, %				
CR or PR / SD	89.2 / 10.8	81.4 / 18.6	86.6 / 13.4	89.0 / 11.0
Prior PCI, %	45.8	61.9	45.4	62.0

Barbie DA. ASCO 2025

ATEZOLIZUMAB

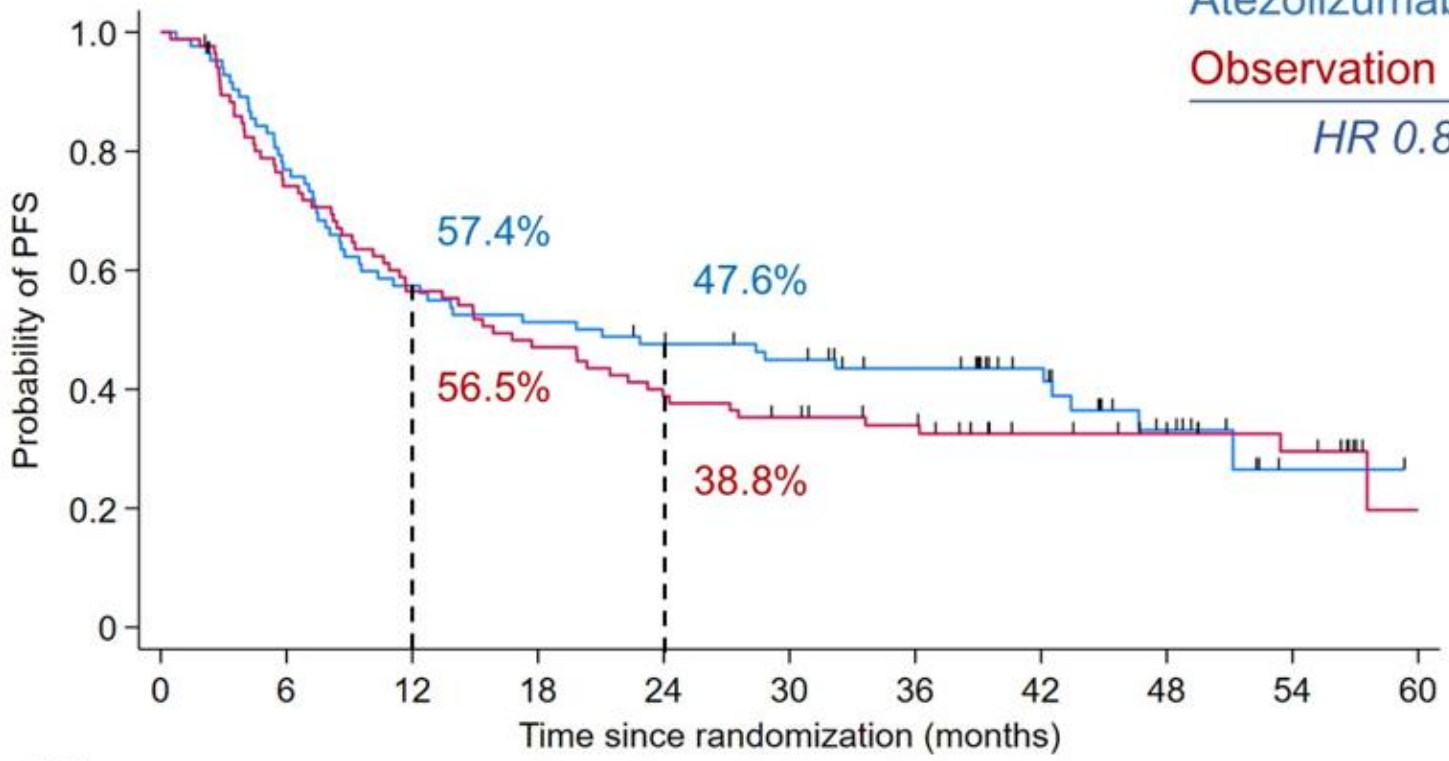


Grønberg BH. ASCO 2025

ATEZOLIZUMAB

	Median	95% CI
Atezolizumab	21.1 months	9.5 – 43.4
Observation	15.9 months	10.6 – 24.0

HR 0.89, 95% CI 0.61 – 1.30, p=0.55

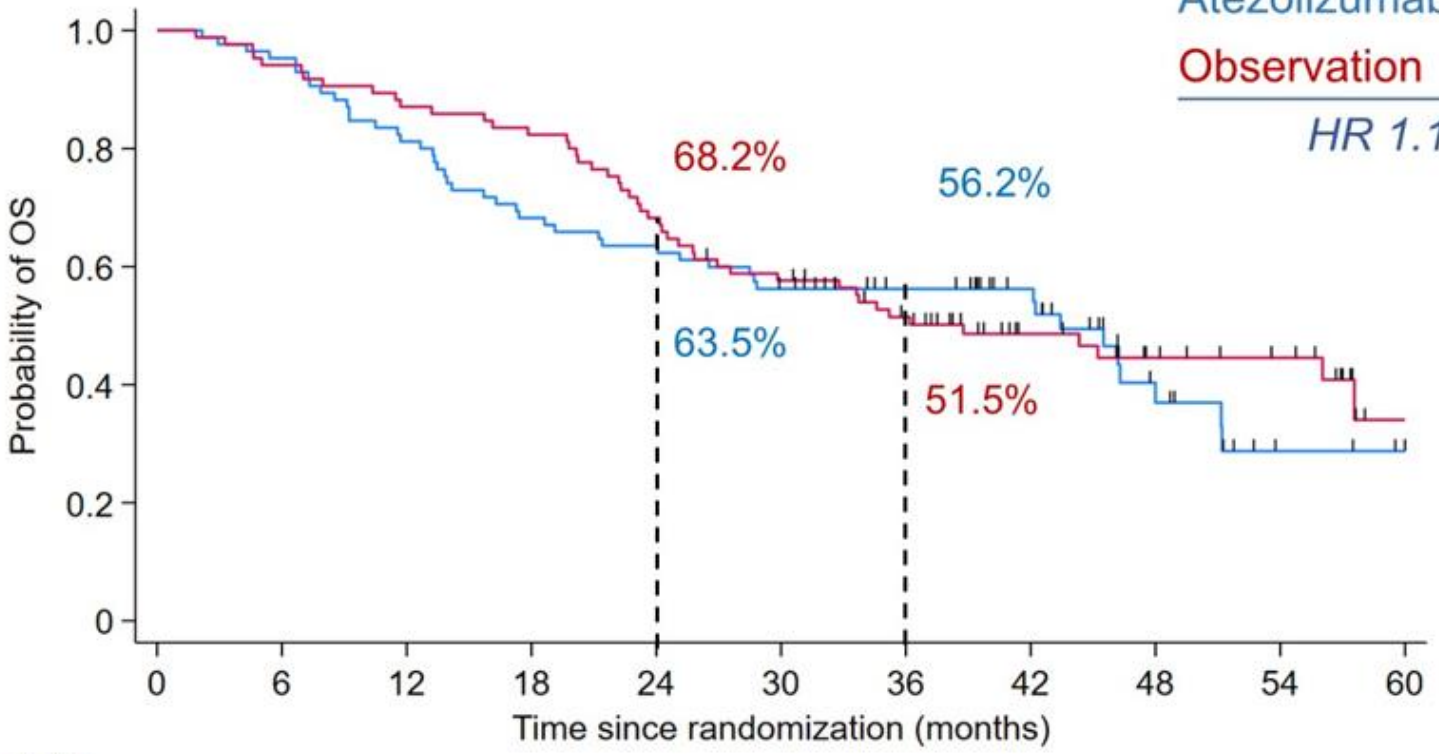


Grønberg BH. ASCO 2025

ATEZOLIZUMAB

	Median	95% CI
Atezolizumab	43.4 months	25.1 – 51.2
Observation	38.8 months	25.8 – 57.6

HR 1.14, 95% CI 0.76 – 1.71, p=0.53



Number at risk

Atezolizumab	85	81	69	58	54	45	36	26	12	3	1
Observation	85	80	74	70	58	49	40	25	18	14	3

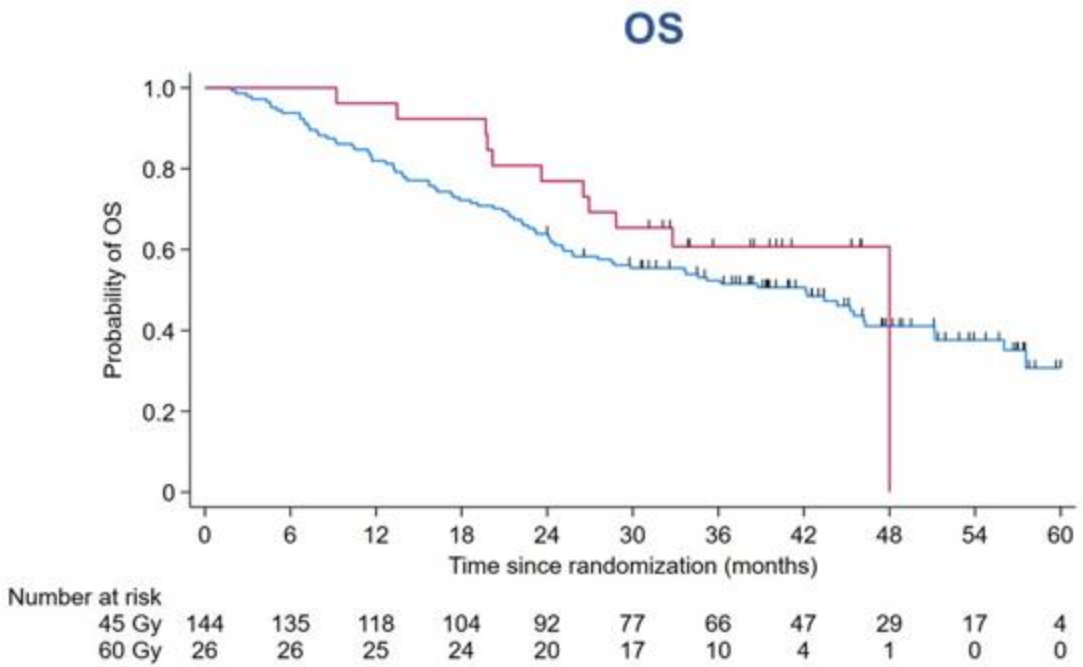
Grønberg BH. ASCO 2025

ATEZOLIZUMAB

	Atezolizumab (n=85)		Observation (n=85)	
	n	%	n	%
Esophagitis	9	10.6%	12	14.1%
Pneumonitis	1	1.2%	2	2.4%
Anemia	12	14.1%	4	4.7%
Neutropenia	27	31.8%	32	37.6%
Thrombocytopenia	6	7.1%	3	3.5%
Neutropenic infection	24	28.2%	21	24.7%
Thrombocytopenic bleeding	1	1.2%	-	-
Infection without neutropenia	5	5.9%	5	5.9%
Nausea	3	3.5%	1	1.2%
Pulmonary embolism	1	1.2%	2	2.4%
Abnormal electrolytes	3	3.5%	-	-
Deep venous thrombosis	1	1.2%	-	-
Cerebral infarction	-	-	1	1.2%
Other	9	10.6%	3	3.5%

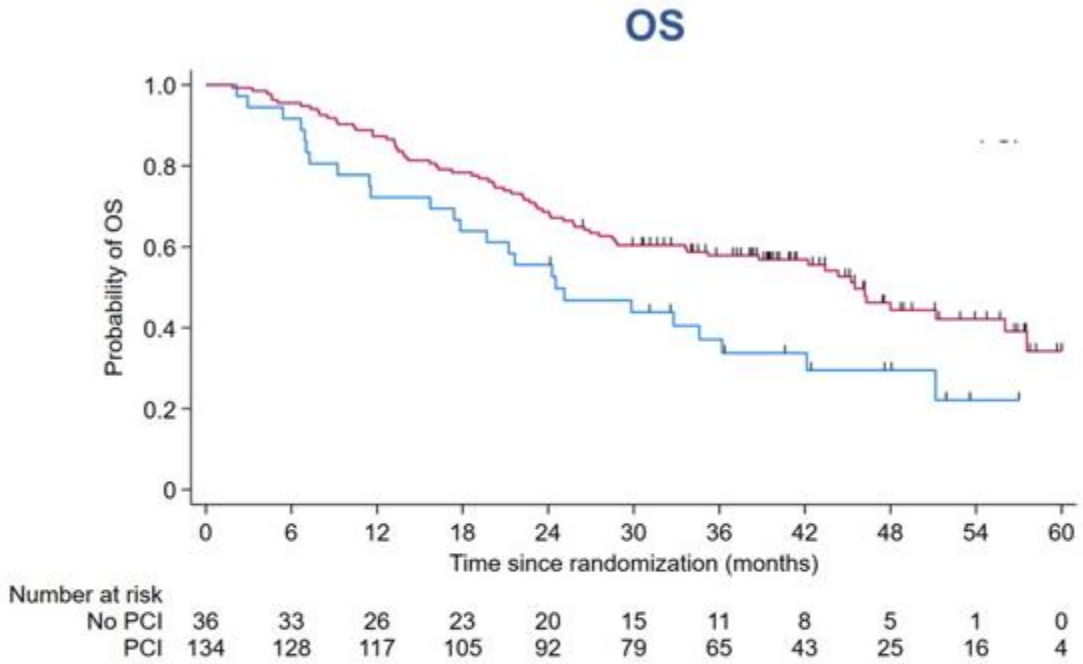
Grønberg BH. ASCO 2025

ATEZOLIZUMAB



	Median	95% CI
45 Gy	42.1 months	25.8 – 46.3
60 Gy	48.0 months	26.9 – NR

HR 0.73, 95% CI 0.39 – 1.37, p=0.33



	Median	95% CI
No PCI	24.5 months	17.4 – 36.2
PCI	45.5 months	33.7 – 57.6

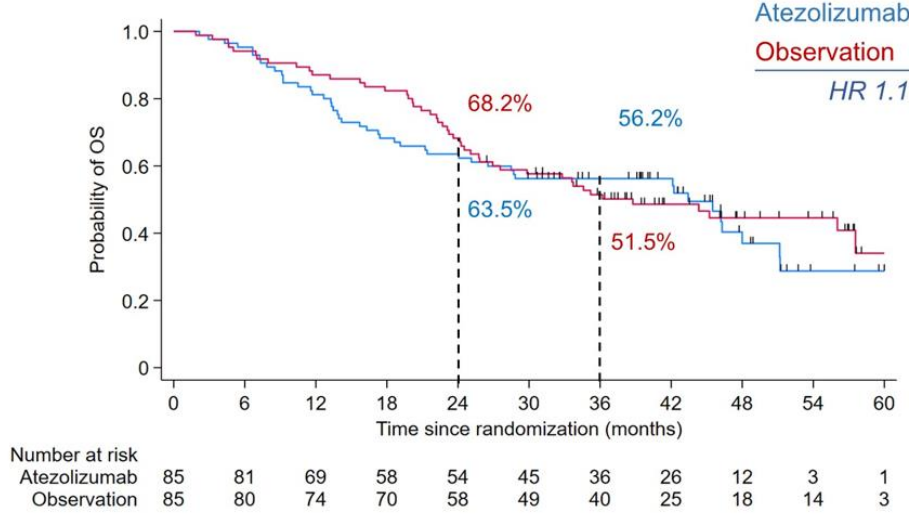
HR 0.57, 95% CI 0.36 – 0.90, p=0.017

Grønberg BH. ASCO 2025

ATEZOLIZUMAB VS DURVALUMAB

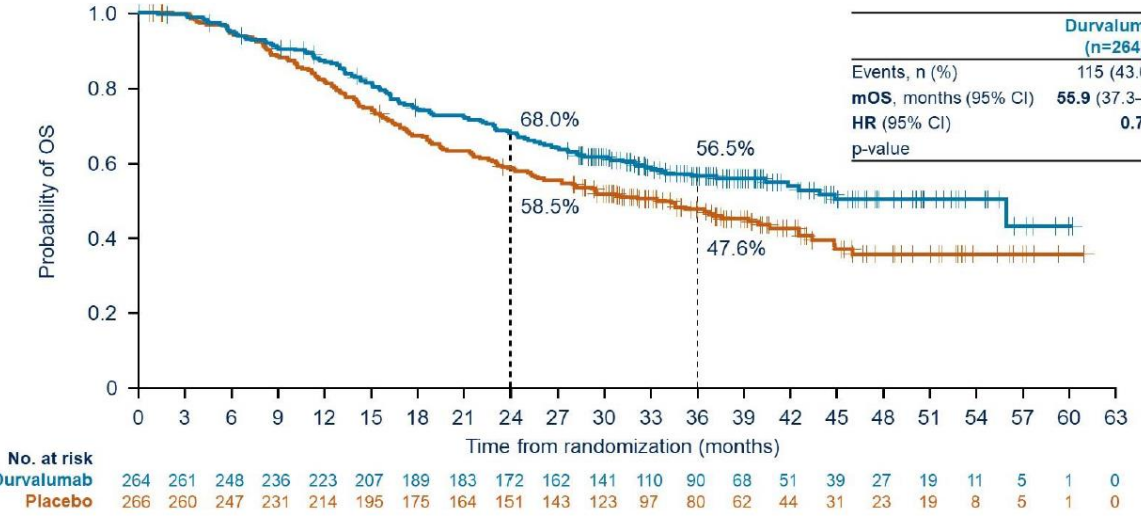
	Median	95% CI
Atezolizumab	43.4 months	25.1 – 51.2
Observation	38.8 months	25.8 – 57.6

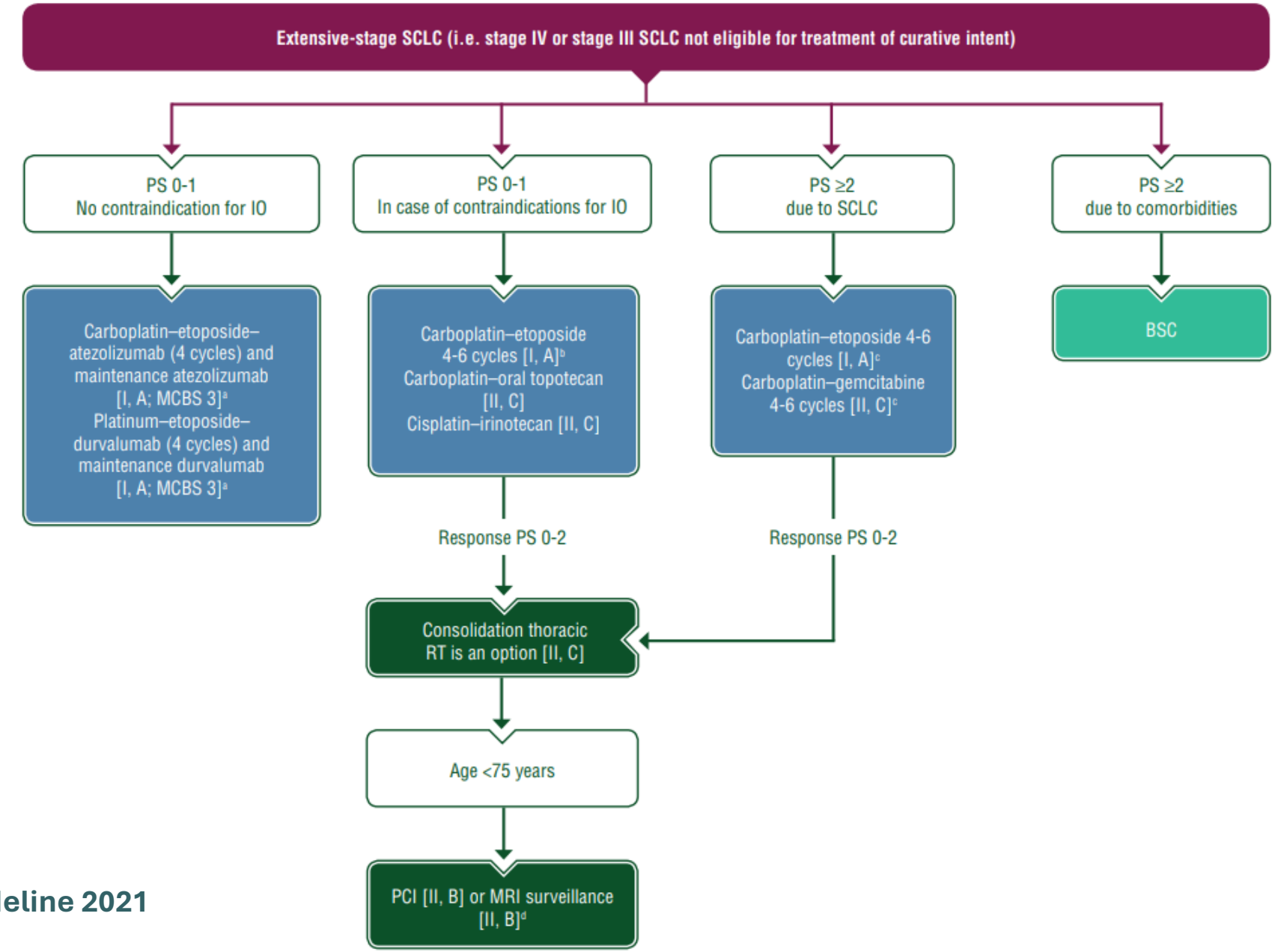
HR 1.14, 95% CI 0.76 – 1.71, p=0.53



Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)

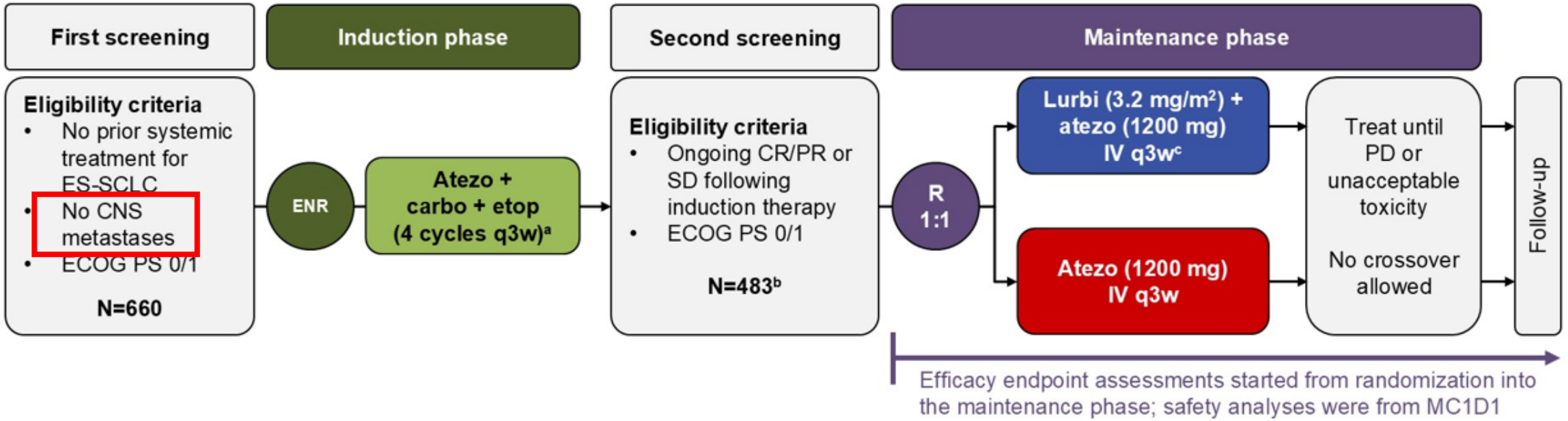
	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

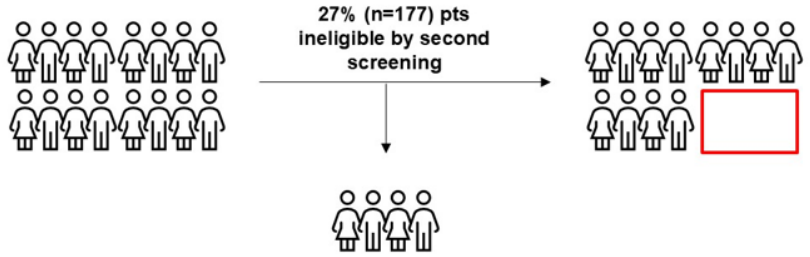




ESMO Clinical Practice Guideline 2021
(Dingemans A.C. Ann Oncol 2021)

IMFORTE





Stratification factors for randomization
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

Primary endpoints
IRF-PFS and OS

Secondary endpoints included
INV-PFS, ORR, DOR, and safety

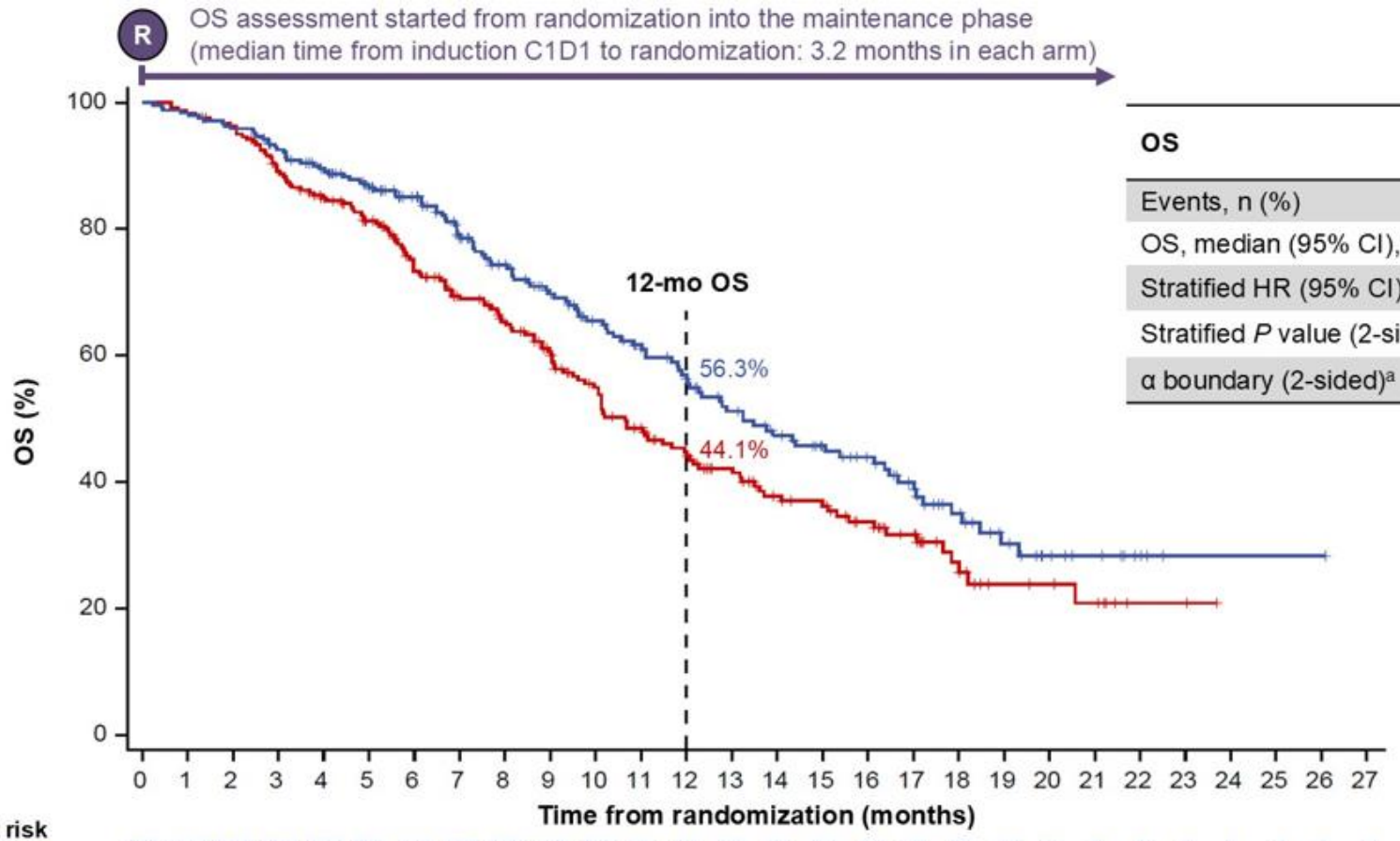
Paz-Ares L. ASCO 2025 + Meador CB. ASCO 2025

IMFORTE

Characteristic	Lurbi + atezo (n=242)	Atezo (n=241)
Age, median (range), years	65.0 (38-85)	67.0 (35-85)
<65 years, n (%)	118 (48.8)	90 (37.3)
Sex, male, n (%)	151 (62.4)	151 (62.7)
Race, n (%)		
White	195 (80.6)	199 (82.6)
Asian	31 (12.8)	31 (12.9)
Other[a]	16 (6.6)	11 (4.6)
Current or previous tobacco use history, n (%)	235 (97.1)	236 (97.9)
Liver metastases at induction BL, n (%)[b]	100 (41.3)	94 (39.0)
Prior PCI, n (%)[b]	34 (14.0)	37 (15.4)
ECOG PS 0 at maintenance BL, n (%)[b]	105 (43.4)	102 (42.3)
LDH ≤ULN at maintenance BL, n (%)[b]	176 (72.7)	179 (74.3)
Time from induction Cycle 1 Day 1 to randomization, median (range), mo	3.2 (2.6-4.6)	3.2 (2.7-5.2)
Response to induction therapy, n (%)[c]		
CR/PR	206 (87.3)	213 (88.8)
SD	28 (11.9)	25 (10.4)
PD[d]	2 (0.8)	2 (0.8)

Paz-Ares L. ASCO 2025

IMFORTE



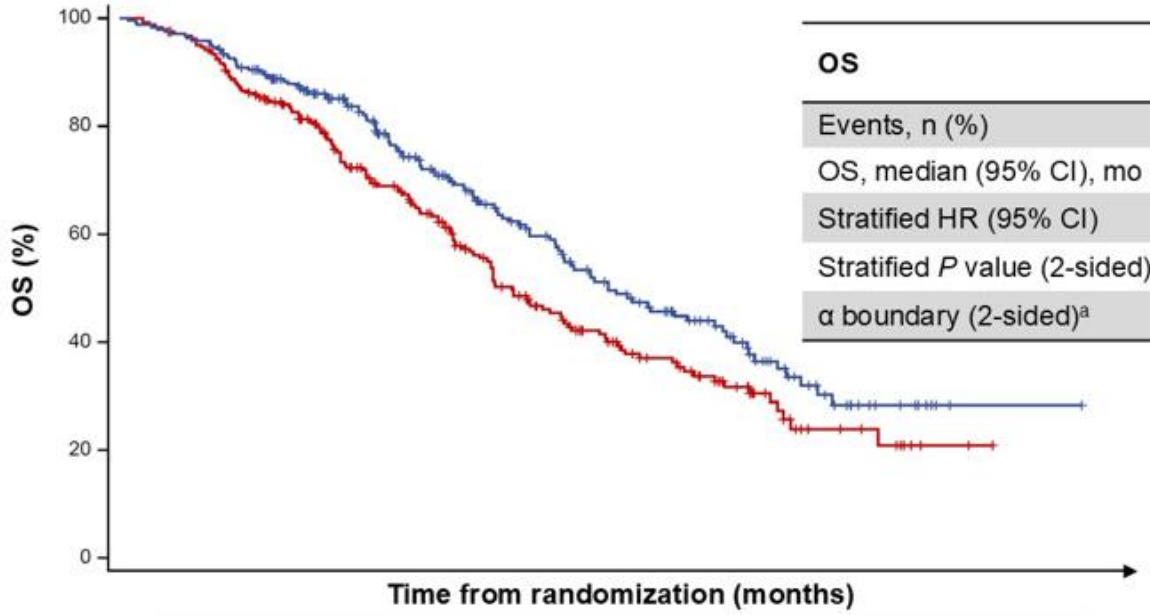
OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).

[a] As determined by the Hwang-Shih-Decani alpha spending function with the gamma parameter of −1.5.

Paz-Ares L. ASCO 2025

IMFORTE



OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Induction treatment
Atezo + carbo + etop

3.2 months[a]

R

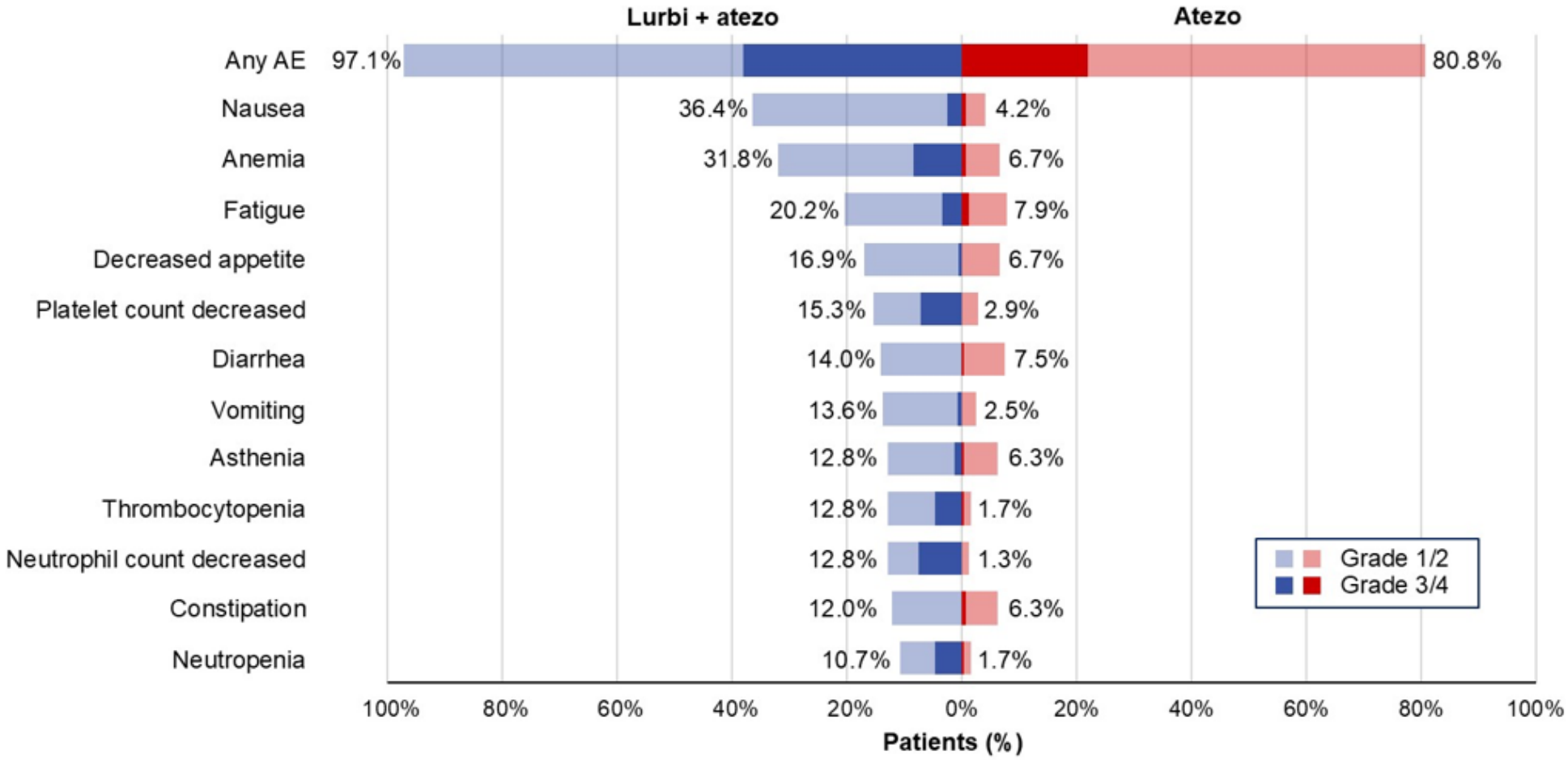
Maintenance treatment
Lurbi + atezo
Median OS from randomization: 13.2 months

Maintenance treatment
Atezo
Median OS from randomization: 10.6 months

IMforte results do not include time on induction treatment

Paz-Ares L. ASCO 2025

IMFORTE

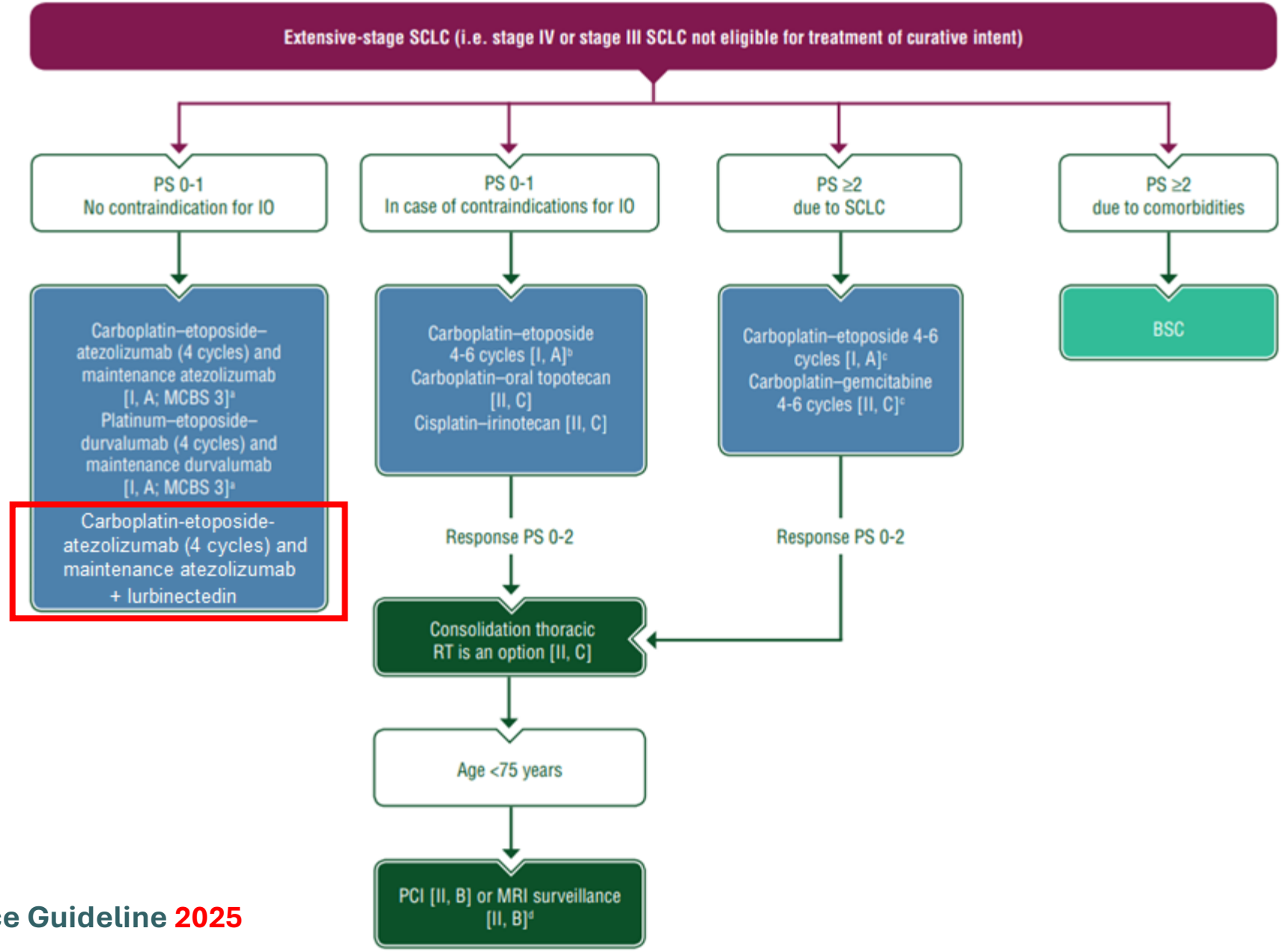


Febrile neutropenia
Lurbi + atezo: 1.7%[a]
Atezo: 0%

Grade 3/4 infections and infestations[b]
Lurbi + atezo: 6.6%
Atezo: 5.0%

All cause AEs with incidence of ≥10% in either arm

Paz-Ares L. ASCO 2025

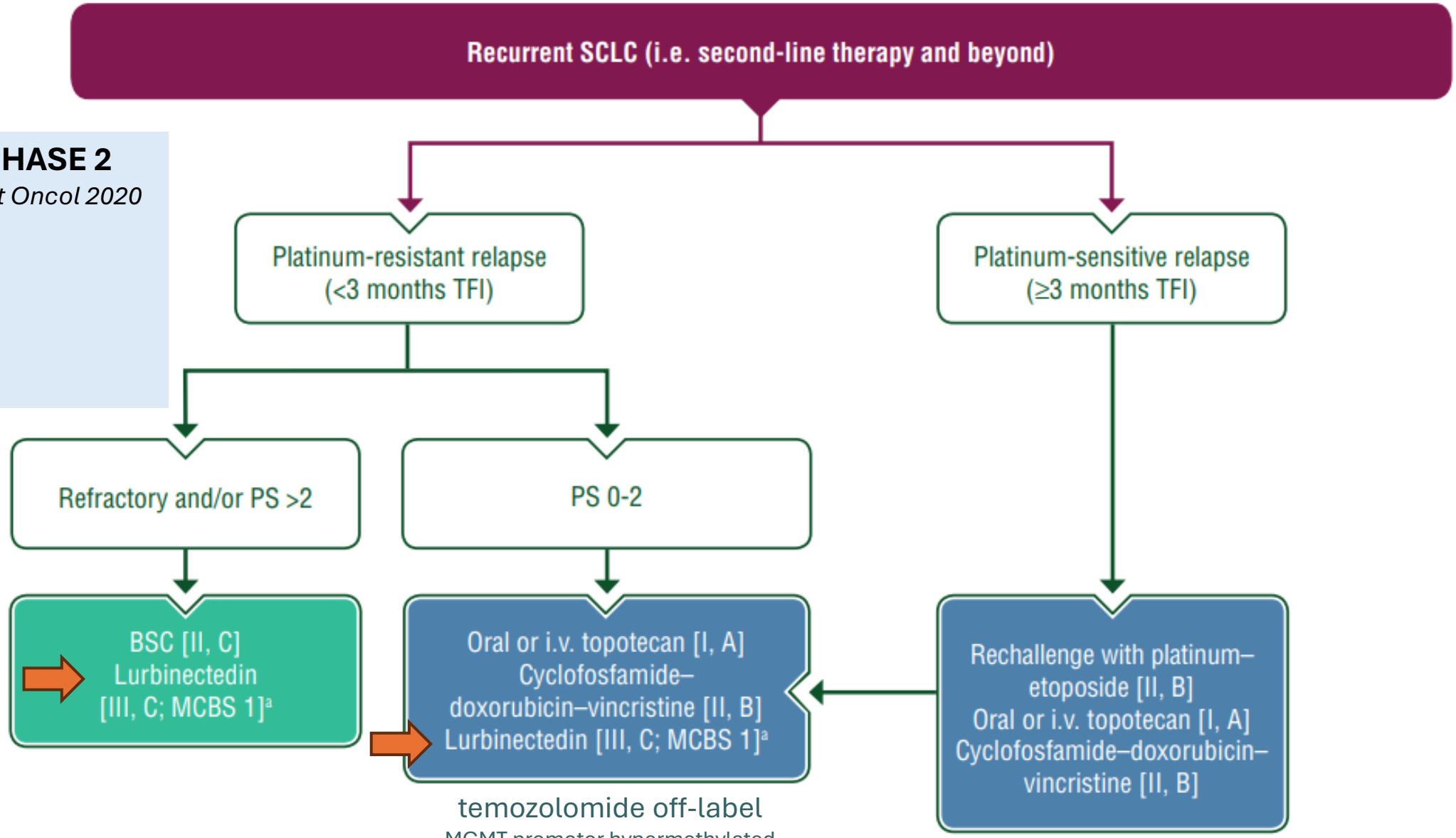


ESMO Clinical Practice Guideline 2025
(hypothetically)

LURBIN. PHASE 2

Trigo J. Lancet Oncol 2020

ORR 35.2%
mPFS 3.5 m
mOS 9.3 m
TRAE G3+ ?



temozolomide off-label
MGMT promotor hypermethylated

ESMO Clinical Practice Guideline 2021
(Dingemans A.C. Ann Oncol 2021)

2SMALL

Non-randomized, open-label phase II study of lurbinectedin plus atezolizumab as second-line therapy for advanced SCLC (NCT04253145)

Key Eligibility Criteria:
- Age ≥ 18 years
- Histologically/cytologically confirmed advanced SCLC
- Progression to 1L platinum based CT ± PD1/PDL1
- CTFI ≥30 days
- Measurable disease
- ECOG PS (0/1)
- Brain metastasis allowed if treated and asymptomatic

SCLC Progression after 1L CT±PD1/PDL1

- Cohort 1: **IO-naïve**
- Cohort 2: **IO-exposed**

RP2D

Lurbinectedin 3.2 mg/m² IV Q3W + Atezolizumab 1200 mg IV Q3W

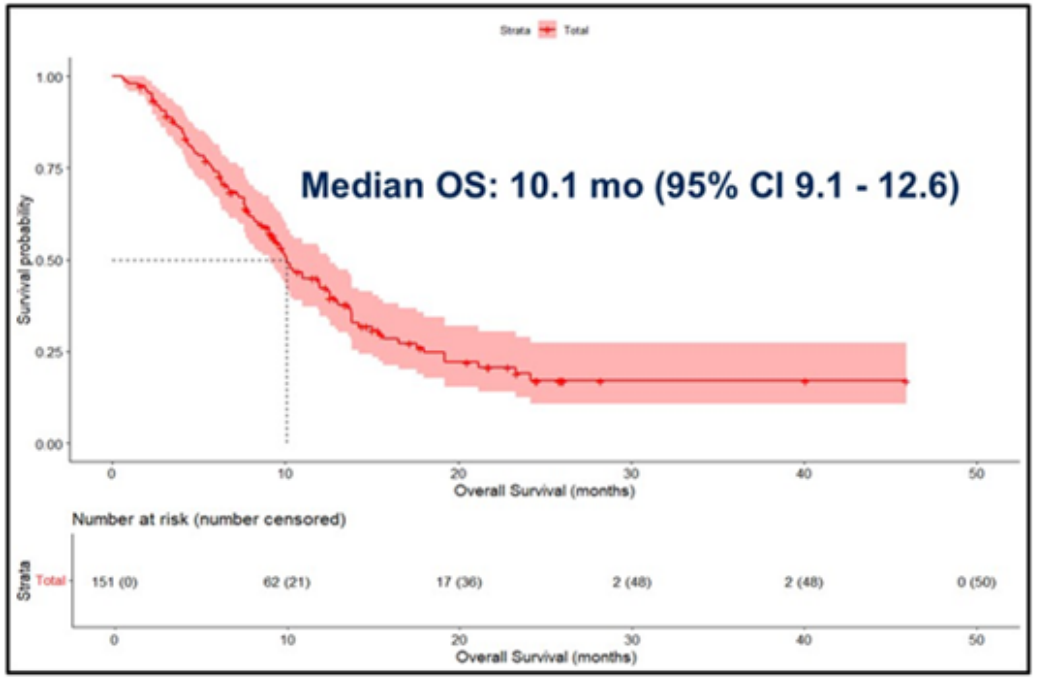
(with prophylactic G-CSF)

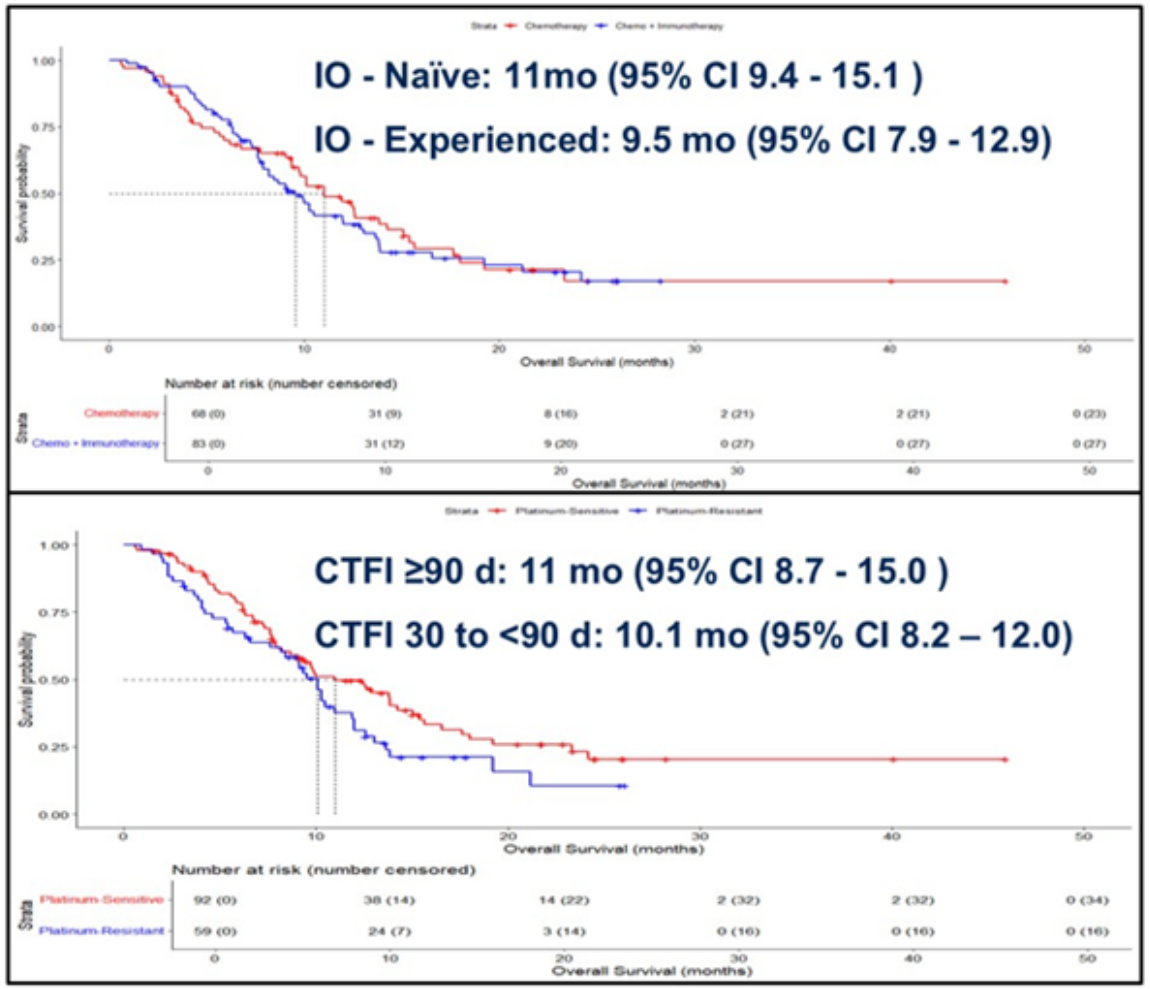
Primary endpoints
- Safety
- ORR (per RECIST v1.1)

Secondary endpoints
- Duration of response (DoR)
- Clinical benefit (CB) CR, PR, SD ≥3 mo)
- PFS
- OS
- Others: PK, PGt and PGx

Ponce Aix S. ASCO 2025

2SMALL





Data cut-off: May 31, 2024. Median follow up for the full analysis set: 9.13 months

Subgroup analyses are descriptive; no formal comparisons were performed

Ponce Aix S. ASCO 2025

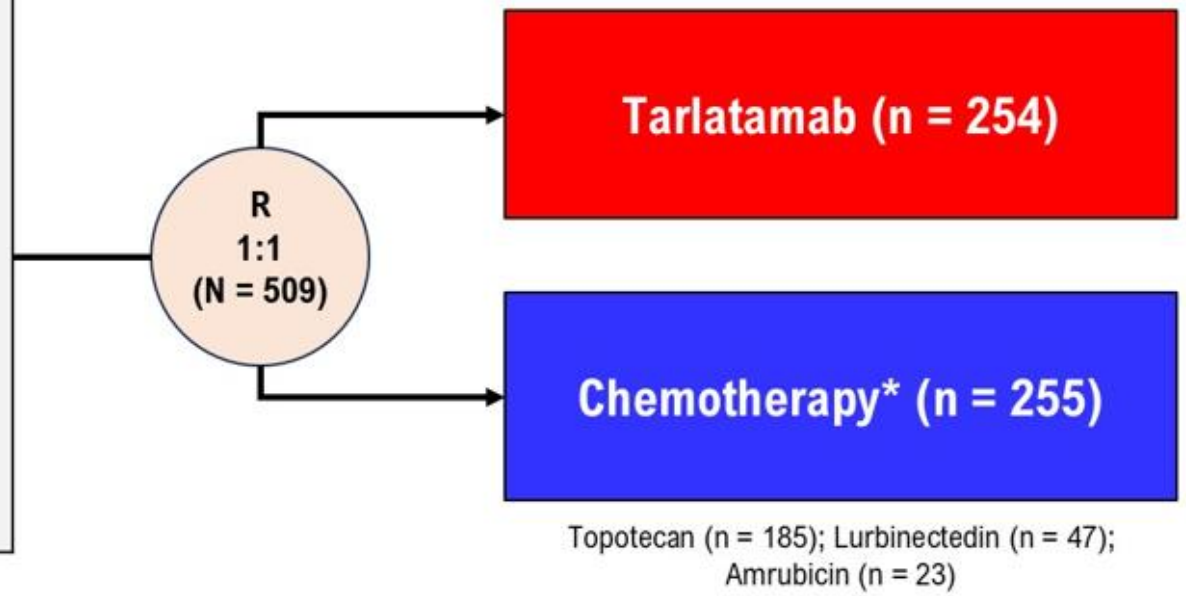
DELLPHI-304

Key inclusion criteria

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

Randomization stratified by

- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)



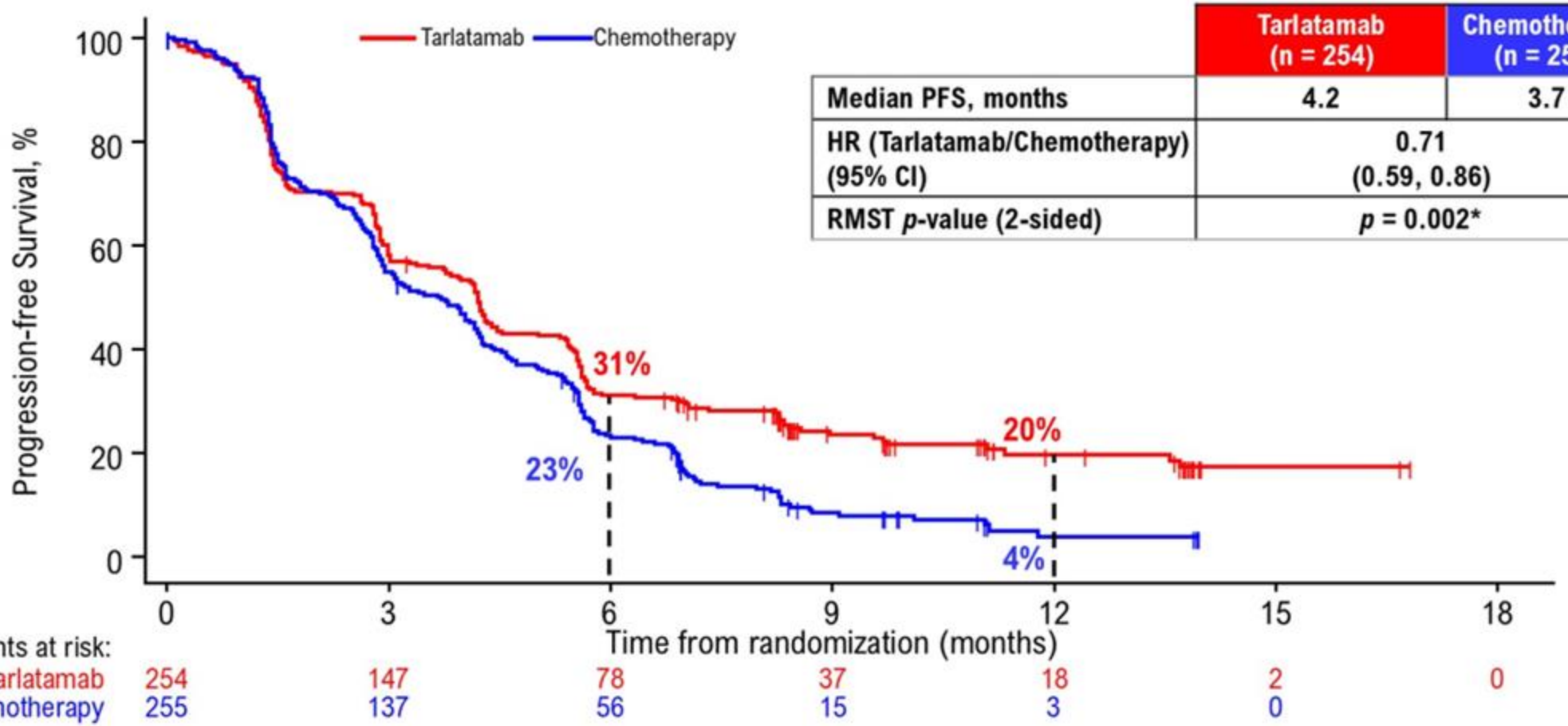
Rudin CM. ASCO 2025

DELLPHI-304

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median age, years (range)	64 (20 – 86)	66 (26 – 84)
Male / Female, %	72 / 28	66 / 34
Race		
Asian / Black / White, %	38 / 1 / 60	42 / 1 / 55
Smoking history		
Current or former smokers / Never smokers, %	91 / 9	88 / 12
ECOG performance status, 0 / 1, %	33 / 67	31 / 68
Prior anti-PD-(L)1 therapy, %	71	71
Prior radiotherapy for current malignancy*, %	63	63
Chemotherapy-free interval,%		
< 90 days	43	45
≥ 90 to < 180 days	33	31
≥ 180 days	24	25
Presence of brain / liver metastases, %	44 / 33	45 / 37
DLL3 expression, %, (n/N†)	95 (207/217)	93 (198/214)

Rudin CM. ASCO 2025

DELLPHI-304

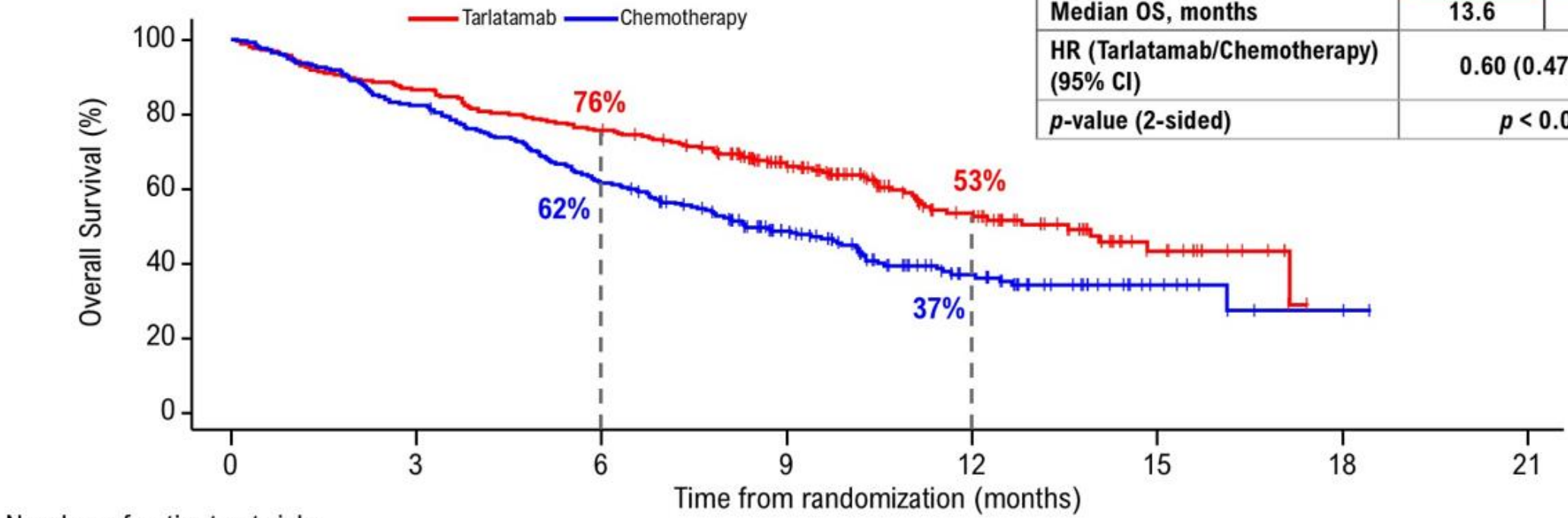


	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

Rudin CM. ASCO 2025

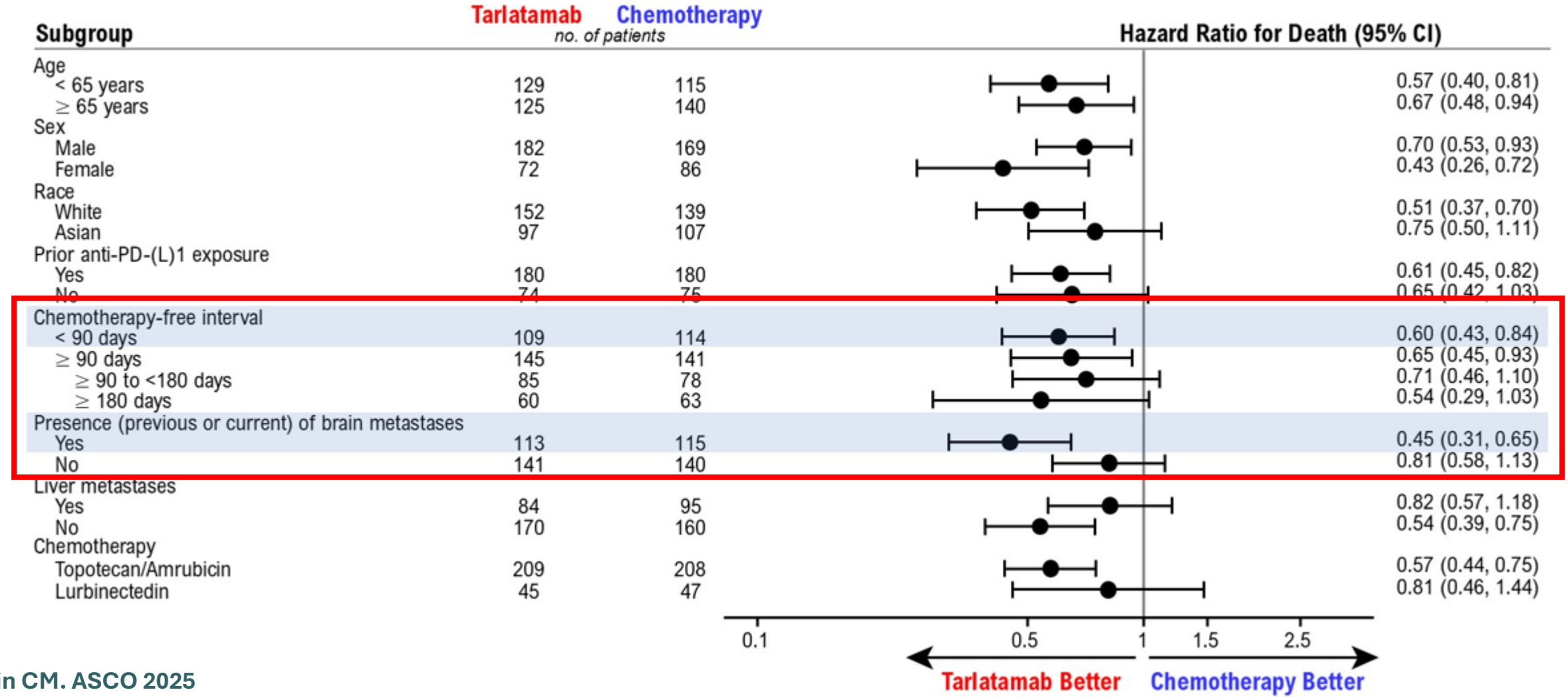
DELLPHI-304

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median OS, months	13.6	8.3
HR (Tarlatamab/Chemotherapy) (95% CI)	0.60 (0.47, 0.77)	
p-value (2-sided)	$p < 0.001$	



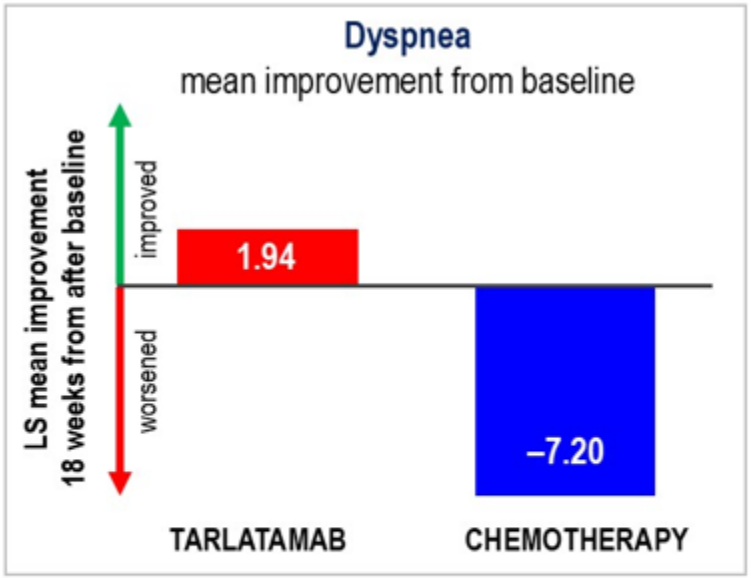
Rudin CM. ASCO 2025

DELLPHI-304

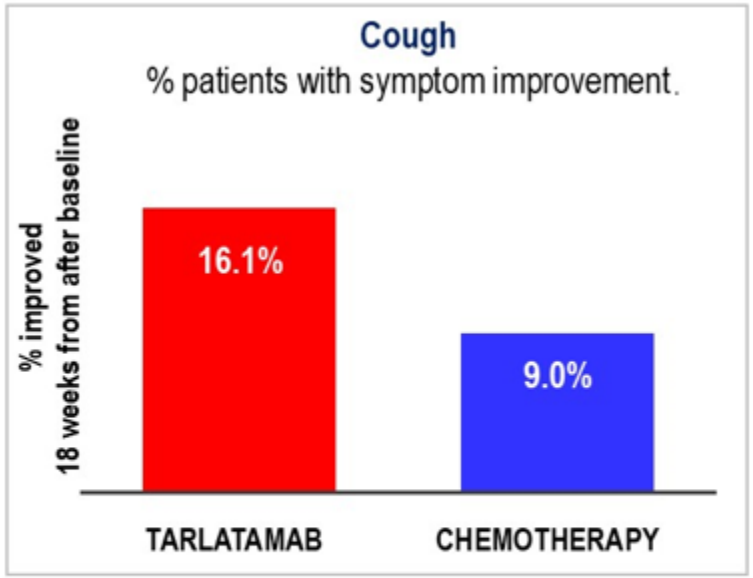


Rudin CM. ASCO 2025

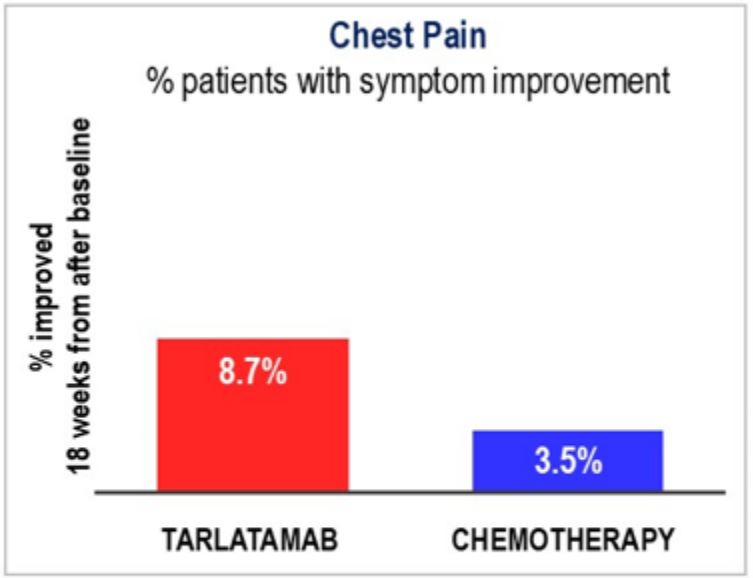
DELLPHI-304



LS mean difference = -9.14*
95% CI (-12.64, -5.64)
p < 0.001



Odds ratio = 2.04*
95% CI (1.17, 3.55)
p = 0.012



Odds ratio = 1.84*
95% CI (0.89, 3.81)
p = 0.1
(Did not meet statistical significance)

Rudin CM. ASCO 2025

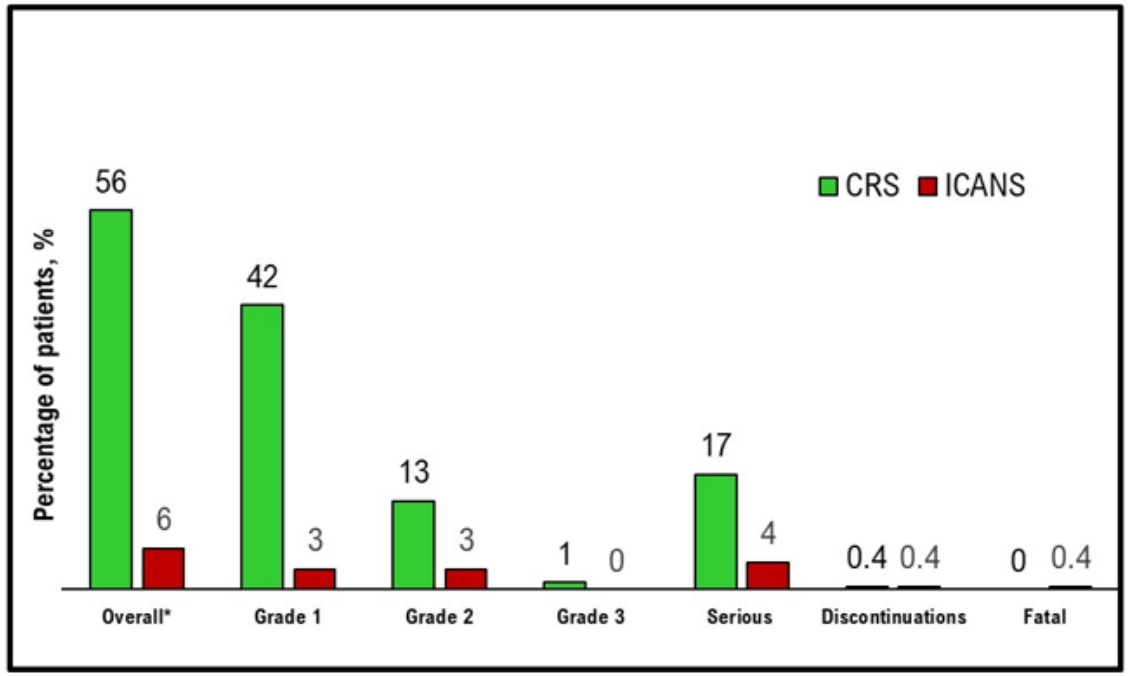
DELLPHI-304

	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose interruption and/or dose reduction, n (%)	48 (19)	134 (55)
TRAEs leading to discontinuation, n (%)	7 (3)	15 (6)
Treatment-related grade 5 events†, n (%)	1 (0.4)	4 (2)

Rudin CM. ASCO 2025

DELLPHI-304

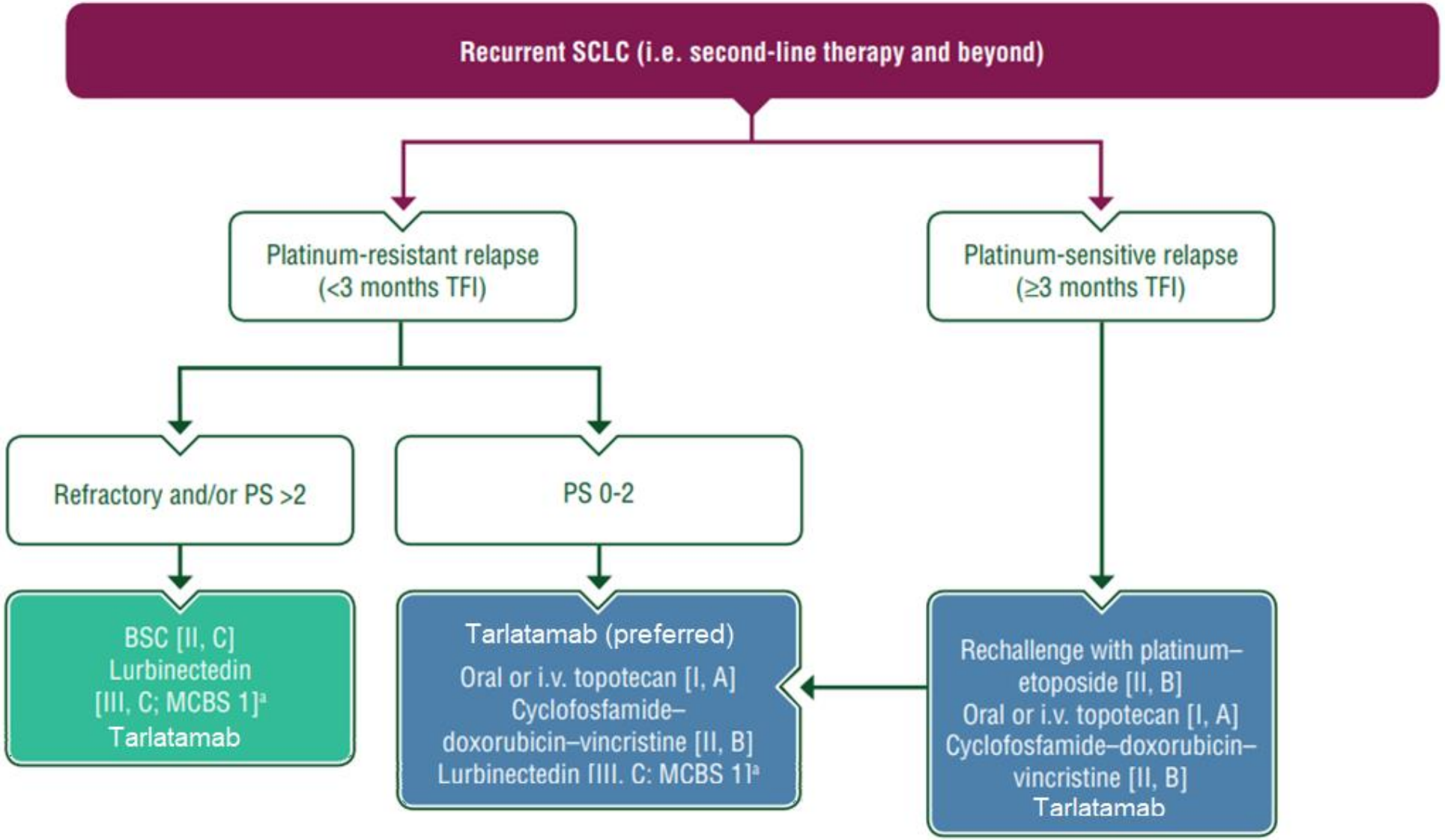
Treatment-emergent CRS and ICANS with tarlatamab



CRS with first two infusions

Tarlatamab (N = 252)	Minimum required monitoring duration: 6 - 8 Hours (n = 43)	Minimum required monitoring duration: 48 Hours (n = 209)
Treatment emergent CRS, n (%)*	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3	0 (0)	3 (1)
Serious adverse events	3 (7)	39 (19)
Leading to discontinuation of IP	0 (0)	1 (0.5)
Median time to intervention from last tarlatamab dose (hours)	17	27

Rudin CM. ASCO 2025



ESMO Clinical Practice Guideline 2025
(hypothetically)

FUTURE PERSPECTIVES

Agent	MOA	Targets	Phase	Indication	Sponsor	Recruiting?
BI 764532	BiTE	DLL3/CD3	1-2	SCLC/NEC	Boehringer	Y
PT217	BiTE	DLL3/CD47	1	SCLC/NEC	Phanes	Y
QLS31904	BiTE	DLL3/CD3	1	SCLC/NEC	Qilu	
HPN328	TriTE	DLL3/CD3/albumin	1-2	SCLC/NEC	Harpoon	Y
RO7616789	TriTE	DLL3/CD3/CD137	1	SCLC/NEC	Roche	N
ZG006	TriTE	DLL3/DLL3/CD3	1-2	SCLC/NEC	Zejing	Y
LB2102	CAR-T	DLL3	1	ES-SCLC LC-NEC	Legend	Y
DLL3-CAR-NK-92	CAR-NK	DLL3	1	SCLC/NEC	Academic*	Y

Meador CB. ASCO 2025

FUTURE PERSPECTIVES

Is earlier tarlatamab better (e.g. first-line ES-SCLC, or LS-SCLC)?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
303	1b	1L ES-SCLC	Tarlatamab + standard therapy	N	NCT05037847
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
306	3	LS-SCLC post-chemoRT	Tarlatamab vs. placebo	Y	NCT06117774
310	1b	1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva	Y	NCT06898957

Is tarlatamab more effective in combination?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
302	1b	2L+ SCLC	Tarlatamab + anti-PD-1 therapy	Y	NCT04184050
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
310	1b	2L SCLC	Tarlatamab + YL201	Y	NCT06898957
		1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva		

Meador CB. ASCO 2025

THYMIC EPITHELIAL TUMOURS

PRESENTED BY: Jo Raskin MD

FIRST-LINE COMBINATION CHEMOTHERAPY REGIMENS[a]

THYMOMA

Preferred (Other Recommended for Thymic Carcinoma)

- **CAP[1]**
  Cisplatin 50 mg/m² IV day 1
  Doxorubicin 50 mg/m² IV day 1
  Cyclophosphamide 500 mg/m² IV day 1
  Administered every 3 weeks

THYMIC CARCINOMA

Preferred (Other Recommended for Thymoma)

- **Carboplatin/paclitaxel[4,5,b]**
  Carboplatin AUC 6 IV day 1
  Paclitaxel 200 mg/m² IV day 1
  Administered every 3 weeks

Preferred (Thymic Carcinoma only)

- **Carboplatin/paclitaxel/ramucirumab[6,c]**
  Ramucirumab 10 mg/kg IV day 1
  Paclitaxel 200 mg/m² IV day 1
  Carboplatin AUC 5 IV day 1
  Administered every 3 weeks, maximum of six cycles
  Ramucirumab monotherapy every 3 weeks as maintenance therapy, until progressive disease or unacceptable toxicity

Other Recommended for Thymic Carcinoma and Thymoma

- **CAP with prednisone[2]**
  Cyclophosphamide 500 mg/m² IV day 1;
  Doxorubicin, 20 mg/m²/day IV continuous infusion days 1–3;
  Cisplatin 30 mg/m²/day IV days 1–3;
  Prednisone 100 mg/day PO days 1–5;
  Administered every 3 weeks

- **ADOC[3]**
  Doxorubicin 40 mg/m² IV day 1;
  Cisplatin 50 mg/m² IV day 1;
  Vincristine 0.6 mg/m² IV day 3;
  Cyclophosphamide 700 mg/m² IV day 4
  Administered every 3 weeks

- **PE[7,b]**
  Cisplatin 60 mg/m² IV day 1;
  Etoposide 120 mg/m²/day IV days 1–3;
  Administered every 3 weeks

- **Etoposide/ifosfamide/cisplatin[8]**
  Etoposide 75 mg/m²/day IV days 1–4;
  Ifosfamide 1.2 g/m²/day IV days 1–4;
  Cisplatin 20 mg/m²/day IV days 1–4
  Administered every 3 weeks

NCCN Clinical Practice Guideline 2.2025

SECOND-LINE SYSTEMIC THERAPY
(regimens noted in alphabetical order)

THYMOMA

Preferred
- Everolimus[9]
- Gemcitabine ± capecitabine[10,11]
- Octreotide[d] (including LAR) (if octreotide scan or dotatate PET/CT positive) ± prednisone[12,13]
- Pemetrexed[14]

Other Recommended
- 5-FU and leucovorin[15]
- Paclitaxel[16]

Useful in Certain Circumstances
- Etoposide[7,17]
- Ifosfamide[18]

THYMIC CARCINOMA

Preferred
- Gemcitabine ± capecitabine[10,11]
- Lenvatinib[e,19]
- Pembrolizumab[f,20,21]
- Sunitinib[22]

Other Recommended
- Avelumab + axitinib[23]
- Everolimus[9]
- 5-FU and leucovorin[15]
- Paclitaxel[16]
- Pemetrexed[14]

Useful in Certain Circumstances
- Etoposide[7,17]
- Ifosfamide[18]

PHASE 2

Giaccone G. Lancet Oncol 2018

ORR 22.5%
mPFS 4.2 m
mOS 24.9 m
TRAE G≥3 ?%

NCCN Clinical Practice Guideline 2.2025

EORTC-ETOP NIVOTHYM

Advanced/relapsed thymic tumor

Type B3 thymoma or thymic carcinoma

No more than one line of platinum-based chemotherapy

No autoimmune disorder

Cohort 1:

Nivolumab
(240 mg IV Q2 weeks)

n=55

Previously published

Cohort 2:

Nivolumab
(240 mg IV Q2 weeks)
+ Ipilimumab
(1 mg/kg IV Q6 weeks)

n=56

Imaging at week 8 and then every 6 weeks

Primary endpoint : PFS rate at 6 months per BICR (RECIST 1.1)

H0: PFSR-6 ≤ 40%
H1: PFSR-6 = 60%

Alpha = 0.1 (one-sided)
Power = 94%

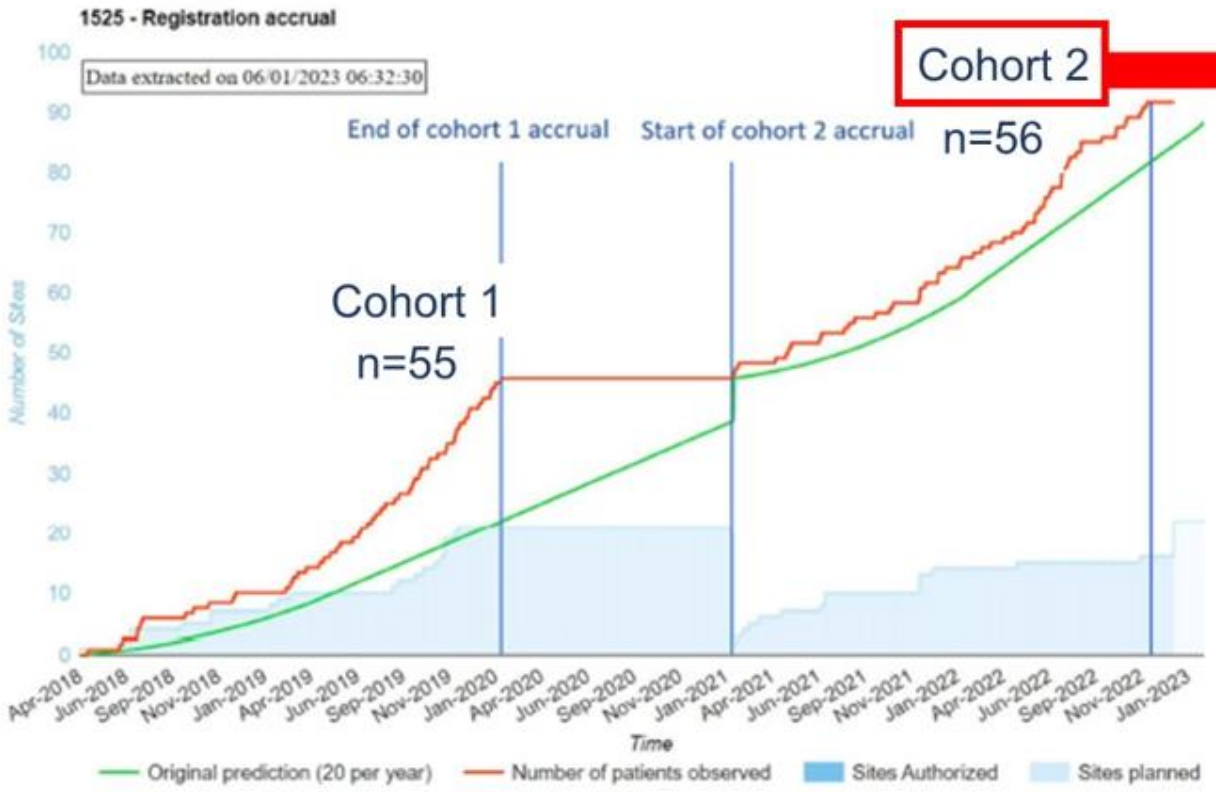
(Girard N. ESMO Open 2023)

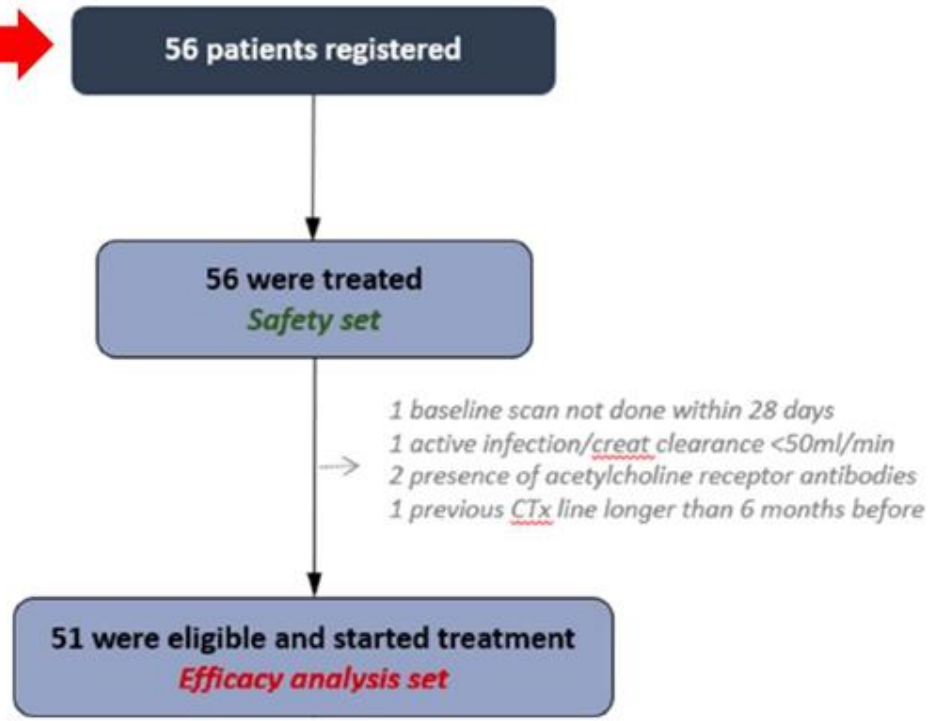
Secondary endpoints: PFSR-6 per local investigator, PFS, Response, OS, Safety

Girard N. ASCO 2025

EORTC-ETOP NIVOTHYM

EORTC and ETOP demonstrated a unique capability in fostering collaboration of 15 centers in 5 European countries to recruit a total of 111 patients in 45 months.





Girard N. ASCO 2025

EORTC-ETOP NIVOTHYM

	Cohort 2 (n=56) n (%)
Median age (range)	64y (34-82)
Gender	
Male	37 (66)
Female	19 (34)
Performance status	
0-1	54 (96)
2	2 (4)
Histological type	
Thymoma (type B3)	8 (14)
Thymic carcinoma	48 (86)
Previous primary tumor resection	33 (59)
Previous chemotherapy for locally-advanced disease	3 (5)

	Cohort 2 (n=56) n (%)
Metastatic sites	
Brain	0 (0)
Lymph nodes	30 (54)
Liver	26 (46)
Lung	26 (46)
Pleura	24 (43)
Bone	26 (46)
Type of progression on last line of treatment	
Locoregional	16 (29)
Distant	25 (45)
Both	14 (25)
Unknown	1 (2)

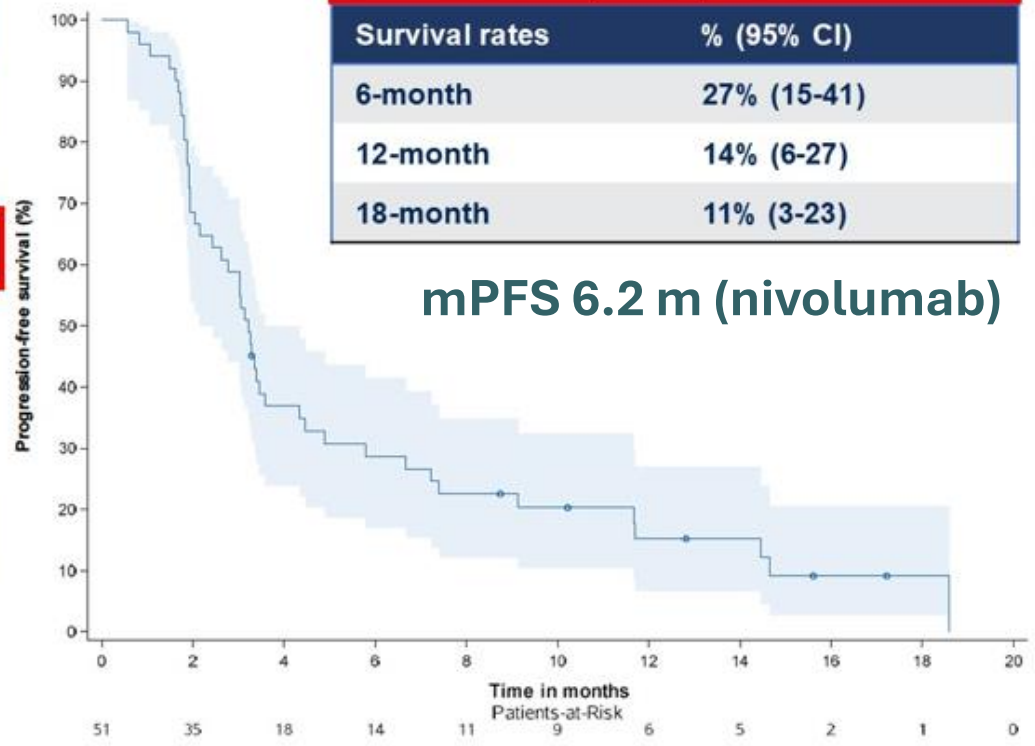
Girard N. ASCO 2025

EORTC-ETOP NIVOTHYM

PFSR-6 by central review	Nivolumab + Ipilimumab (n=51) Per protocol population n (%)
PFSR-6	**PFS-R6 35% (nivolumab)**
Failure	40 (78%)
Success	11 (22%)
Reason failure at 6 months	
Progressive disease (PD)	27 (68)
Death before PD	3 (8)
Start further therapy before PD	4 (10)
Missing disease evaluation at 6 months	6 (15)

Median Follow-up 16.1 months

Median PFS: 3.1 (2.0-3.6) months	
Survival rates	% (95% CI)
6-month	27% (15-41)
12-month	14% (6-27)
18-month	11% (3-23)



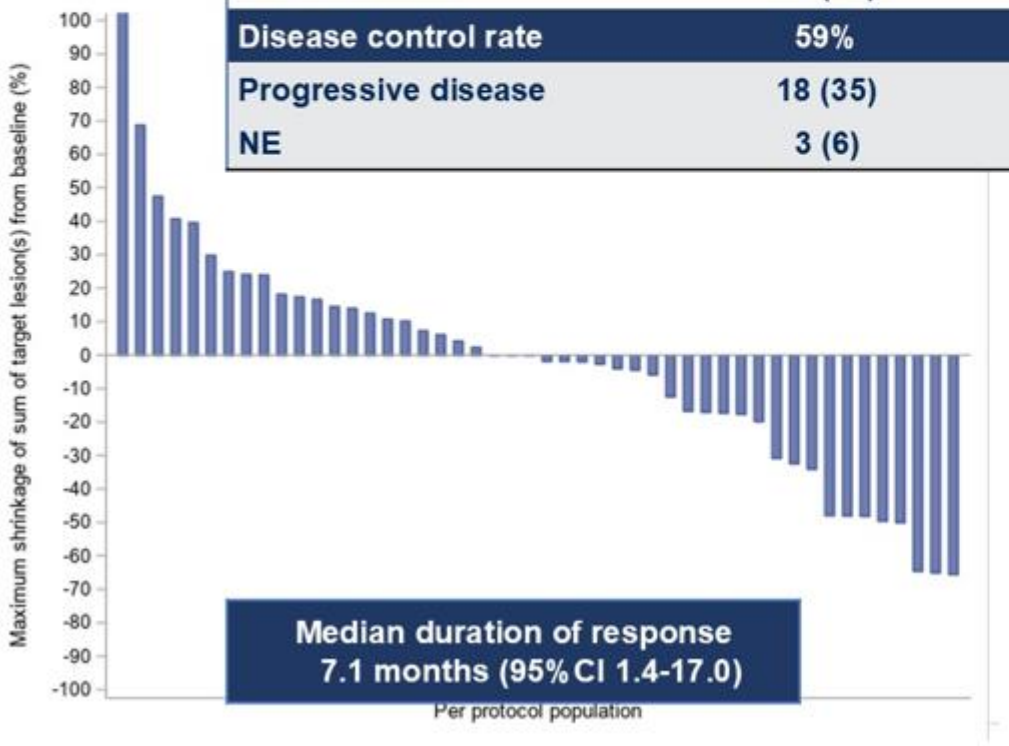
mPFS 6.2 m (nivolumab)

Girard N. ASCO 2025

EORTC-ETOP NIVOTHYM

Objective response

	Nivolumab + Ipilimumab (n=51) n (%)
Partial response	8 (16)
Stable disease	22 (43)
Disease control rate	59%
Progressive disease	18 (35)
NE	3 (6)



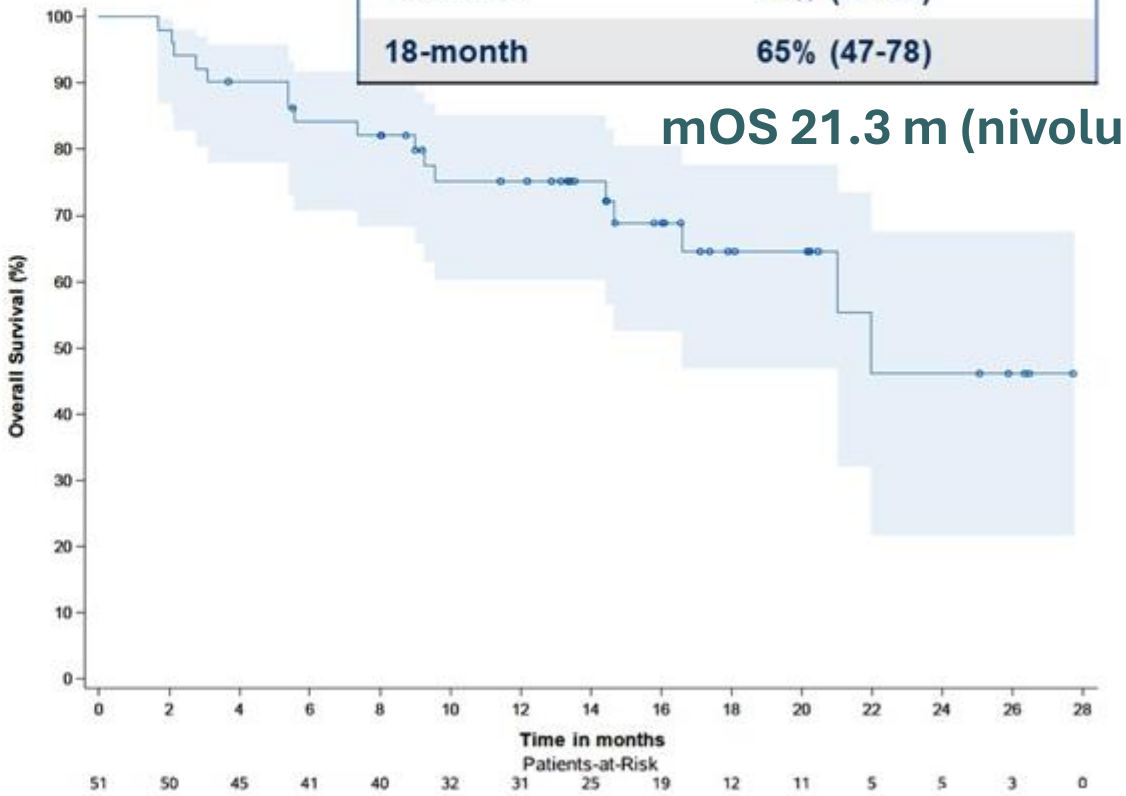
Median duration of response
7.1 months (95% CI 1.4-17.0)

Overall survival

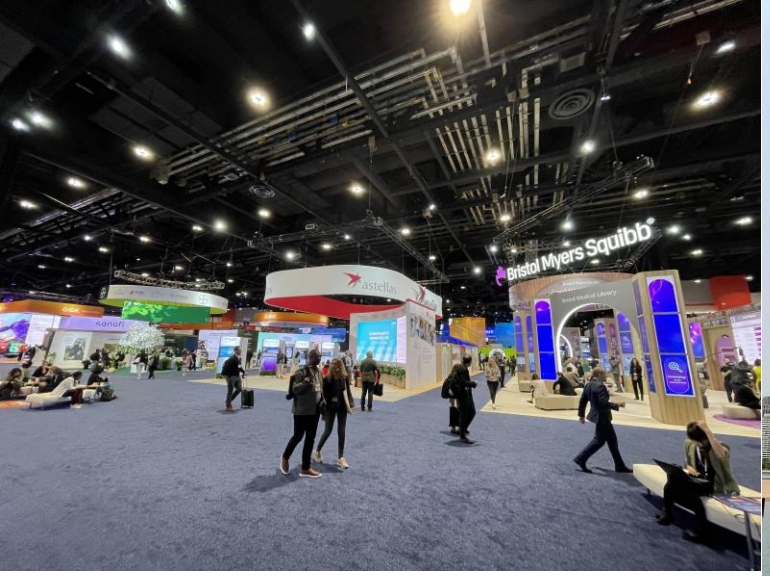
Median OS: 22.0 (16.6-NE) months

Survival rates	% (95% CI)
6-month	84% (71-92)
12-month	75% (60-85)
18-month	65% (47-78)

mOS 21.3 m (nivolumab)



Girard N. ASCO 2025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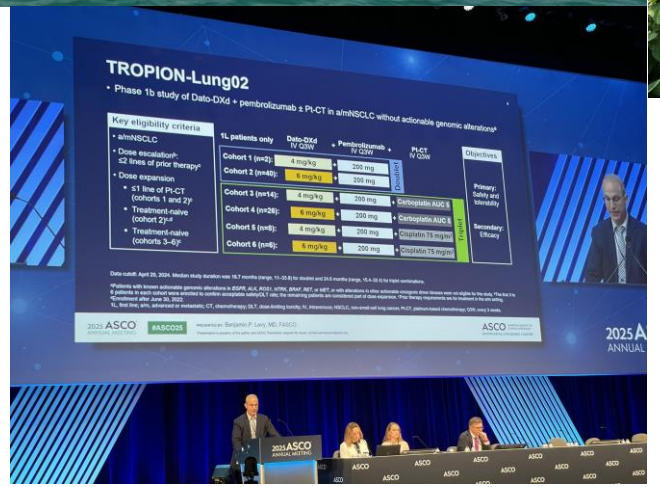
TROPION-Lung02
• Phase 1b study of Dato-DXd + pembrolizumab ± Pt-CT in a/mNSCLC without actionable genomic alterations
Key eligibility criteria
• a/mNSCLC
• Dose escalation: ≤2 lines of prior therapy
• Dose expansion
1L patients only
Dato-DXd IV Q3W
+ Pembrolizumab IV Q3W
Pt-CT IV Q3W
Cohort 1 (n=2):
Cohort 2 (n=40):
Cohort 3 (n=14):
Cohort 4 (n=26):
Cohort 5 (n=6):
Cohort 6 (n=6):
4 mg/kg
6 mg/kg
200 mg
Carboplatin AUC 5
Cisplatin 75 mg/m²
Objectives
Primary: Safety and tolerability
Secondary: Efficacy
#ASCO25