ETOP·IBCSG
PARTNERS FOUNDATION

Foundation for International
Cancer Research

AACR Annual Meeting 2025

April 25–30, 2025

Supported by Eli Lilly and Company, BeiGene, GSK and Johnson&Johnson
None of these companies have influenced the content of this publication

GOLD SPONSOR | Lilly

SILVER SPONSORS | BeiGene | GSK | Johnson&Johnson

Letter from Prof Rolf Stahel

Dear Colleagues

It is my pleasure to present this ETOP slide set which has been designed to highlight and summarise key findings in thoracic cancers from the major congresses in 2025. This slide set specifically focuses on the **AACR Annual Meeting 2025** and is available in 3 languages – English, Chinese and Japanese.

The area of clinical research in oncology is a challenging and continually changing environment. Within this environment we all value access to scientific data and research which helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in thoracic cancers of benefit to you in your practice. If you would like to share your thoughts with us, we would welcome your comments. Please send any correspondence to etop@etop.eu-org.

I would like to thank our ETOP members Drs Enriqueta Felip and Solange Peters for their roles as Editors – for prioritising abstracts and reviewing slide content. The slide set you see before you would not be possible without their commitment and hard work.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this complex yet rewarding activity.

Yours sincerely,
Rolf Stahel
President, ETOP Foundation Council

ETOP Medical Oncology Slide Deck Editors 2025

Focus: Advanced NSCLC (not radically treatable stage III and stage IV) and biomarkers (all stages)

Dr Solange Peters

Multidisciplinary Oncology Center, Lausanne Cancer Center, Lausanne, Switzerland

Focus: Early and locally advanced NSCLC (stage I–III) and other malignancies, SCLC, mesothelioma, rare tumours

Dr Enriqueta Felip

Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Contents

- Screening, biomarkers and prevention
- Early stage and locally advanced NSCLC – Stages I, II and III
- Advanced NSCLC – Not radically treatable stage III and stage IV
  - Immunotherapy
  - Targeted therapies
  - ADCs and other therapies

Screening, biomarkers and prevention

3815: High-penetrance rare variants underlying familial lung cancer risk: Insights from the Genetic Epidemiology of Lung Cancer Consortium – Liu Y, et al

- **Study objective**
  - To identify high-penetrance rare, pathogenic germline variants and evaluate their role in familial lung cancer

- **Methods**
  - Whole-genome and exome sequencing was conducted in 129 families with high-risk familial lung cancer (FLC), defined as having 2 first-degree or ≥3 second-degree relatives affected by lung cancer (177 affected FLC and 309 unaffected relatives)
  - The aim was to identify rare (allele frequency <1% in Genome Aggregation Database [gnomAD] global population) and deleterious variants (missense, stop-gained, frameshift) that are enriched in FLC
  - External validation of promising variants was conducted using 2408 sporadic lung cancer cases and 885 population controls from the International Lung Cancer Consortium

	Identification		Validation		
Source	**GELCC**	**gnomAD**	**Internal**	**UK Biobank**	**All of Us**
Cases/Controls, n	177 cases	807,162 controls	2408/885	4902/343,753	2775/268,332
Meta-analysis fixed model	Identified: 118 variants			Validated: 53 variants	
Combined: 52 variants across 35 genes 65% missense, 15% stop gained, 6% splicing, 14% frameshift 6 pathogenic, 27 conflict, 8 uncertain					

3815: High-penetrance rare variants underlying familial lung cancer risk: Insights from the Genetic Epidemiology of Lung Cancer Consortium – Liu Y, et al

- **Key results (cont.)**

Top 16 new variants

Function	Gene	Variants	FLC/Relative/ Validation, n	OR combined/ MAF gmonAD
Mucin	GALNT6	p.R195X*	4/1/9	89/0.000008
ERBB2	MUC4	p.D4327T fs 100*	2/3/2	77/0.000007
Skin barrier Inflammation	FLG	p.R3009X*#	3/4/22	88/0.00004
		p.Y3105X*	4/2/4	85/0.00001
		p.W3333X*	2/5/0	72/0.00001
		p.R3404G fs 51*	7/2/3	59/0.0000001
Tumor suppressor	WNK1	p.K583S fs 11*	4/0/23	86/0.00008
	LRP1B	p.S1014P	2/4/1	28/0.00002
	ASXL1	p.G641W fs 12*#	2/5/30	4.5/0.0004
	CFTR	p.R74W	4/2/30	2.0/0.0009
DNA repair	CHD2	p.K1245N fs 4*#	6/0/22	86/0.00008
	MLH1	p.V180G	2/5/3	18/0.00005
Oncogene JAK1	ERC1	p.R708Q	3/1/65	9.6/0.0004
	ERBB3	p.A1131T	3/1/19	2.4/0.0005
Immune response	JAK1	p.V651M	2/3/45	4.0/0.001
	PIM1	p.E124Q	3/1/84	3.0/0.003

New variants in known genes and linkage region

Function	Gene	Variants	FLC/Relative/ Validation, n	OR combined/ MAF gmonAD
Known susceptibility genes				
Tumor suppressor Inflammation	BRCA2	p.N986K fs 2*#	2/0/22	86/0.000002
	ATM	p.D1853V	4/0/83	1.8/0.005
		p.S2146T	2/0/26	1.9/0.003
Linkage 6q22-25				
Tumor suppressor	PRKN	p.Q34R	4/0/31	3.6/0.002
		3'UTR NMD#	5/3/87	2.1/0.003
	LAMA2	p.R2383X*#	2/2/0	75/0.000008
		p.G2472V	2/0/40	63/0.0002
		p.A3054E	2/0/29	66/0.00009
	SYNE1	p.R4673Q	3/2/15	19/0.00009
		p.S6763L	3/1/17	5.4/0.0002
Oncogene	ROS1	Splice acceptor	2/0/20	23/0.00004
		p.F1433S	3/1/34	4.3/0.0007

Red, gain-of-function genes; blue, ultra-rare, large-effect variants;
*protein truncating; #pathogenic clinical variant; fs, frameshift

3815: High-penetrance rare variants underlying familial lung cancer risk: Insights from the Genetic Epidemiology of Lung Cancer Consortium – Liu Y, et al

- **Key results (cont.)**

Gene burden test

Gene	Variants in gene, n	Carriers in FLC/ Internal controls, n	p-value
GALNT6	11	31/0	**8.3E-16**
LAMA2	22	52/26	**9.9E-16**
KIF26B	9	22/1	**1.2E-14**
ROS1	7	21/5	**3.7E-10**
SYNE1	21	52/54	**1.3E-09**
PRKN	5	17/5	**9.0E-09**
PIM1	5	14/2	**2.2E-08**
CHD2	4	12/2	**2.2E-08**
WNK1	4	10/2	**6.4E-07**
FLG	11	55/42	5.2E-06
JAK1	3	6/0	2.0E-05
MUC4	22	180/454	8.4E-05
MLH1	4	13/13	0.00032
ATM	4	11/13	0.000069
CFTR	4	12/7	0.00115

Variant-enriched carriers in high-risk FLC families

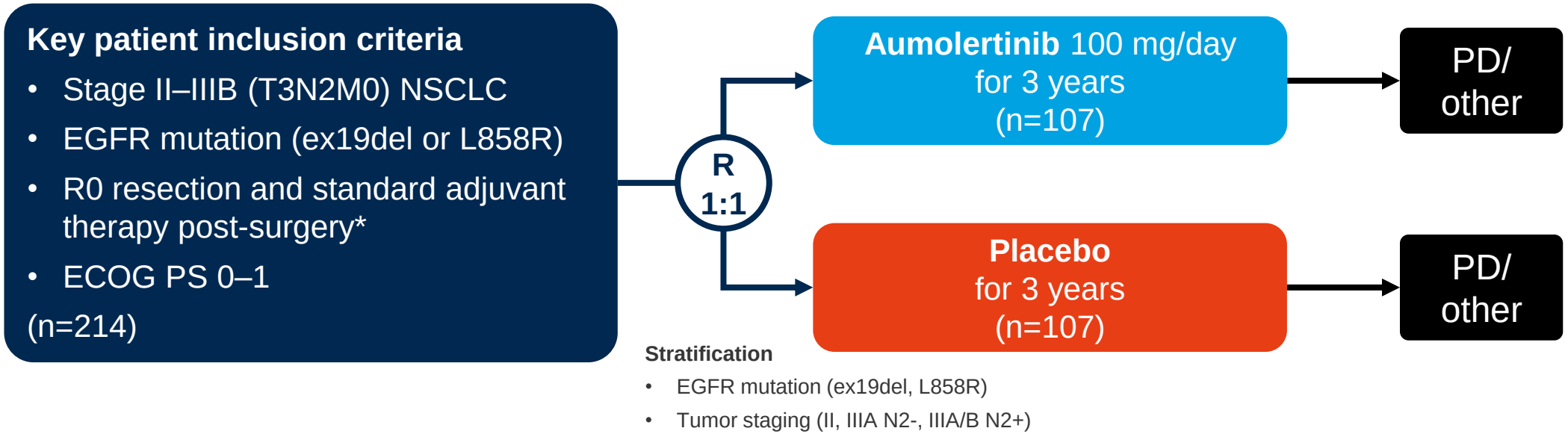
Family	Affected, n	Sequences carriers (characteristics)	Primary variant
KCI110	9	3 FLCs/2 relatives (Black)	FLG, MUC4, MUC19
MCO721	7	2 FLCs (young onset <50 years, female)	6q22-25
KCI487	6	3 FLCs/1 relative (Black)	GALNT6 6q22-25

- **Conclusions**
  - Rare, high-penetrance variants were found to have a significant role in FLC etiology and are different by ancestry with a rate higher in Africans

Early stage and locally advanced NSCLC – Stages I, II and III

CT126: Aumolertinib as adjuvant therapy in patients with stage II-IIIB EGFR-mutated NSCLC after complete tumor resection: A randomized, double-blind, placebo-controlled, phase 3 trial (ARTS) – Cheng Y, et al

- **Study objective**
  - To evaluate the efficacy and safety of adjuvant aumolertinib, an EGFR TKI, in patients with stage II–IIIB, EGFR-mutated NSCLC in the phase 3 ARTS trial in a Chinese population



Primary endpoint

- DFS (BICR)

Secondary endpoints

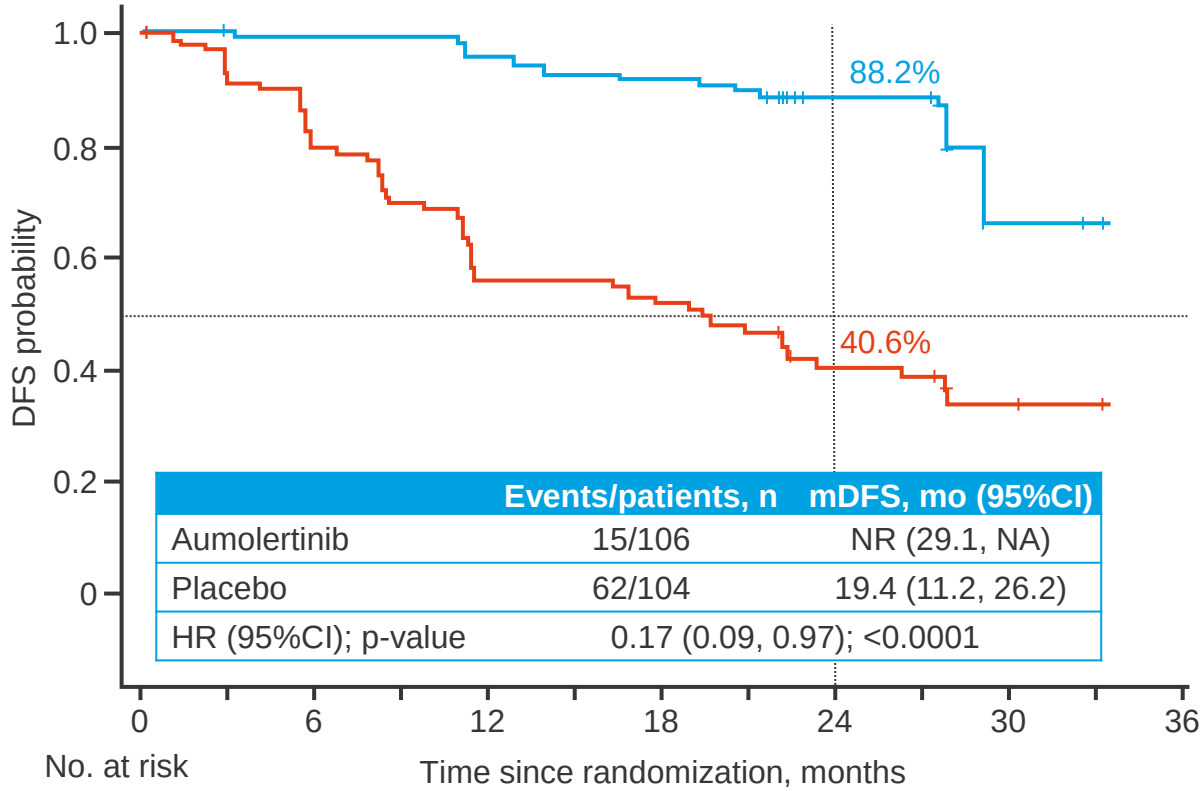
- DFS (investigator), OS, PK, safety

*Patients with stage IIA disease could receive chemotherapy and patients with stage IIB–IIIB had to have received platinum-based doublet adjuvant chemotherapy

CT126: Aumolertinib as adjuvant therapy in patients with stage II-IIIB EGFR-mutated NSCLC after complete tumor resection: A randomized, double-blind, placebo-controlled, phase 3 trial (ARTS) – Cheng Y, et al

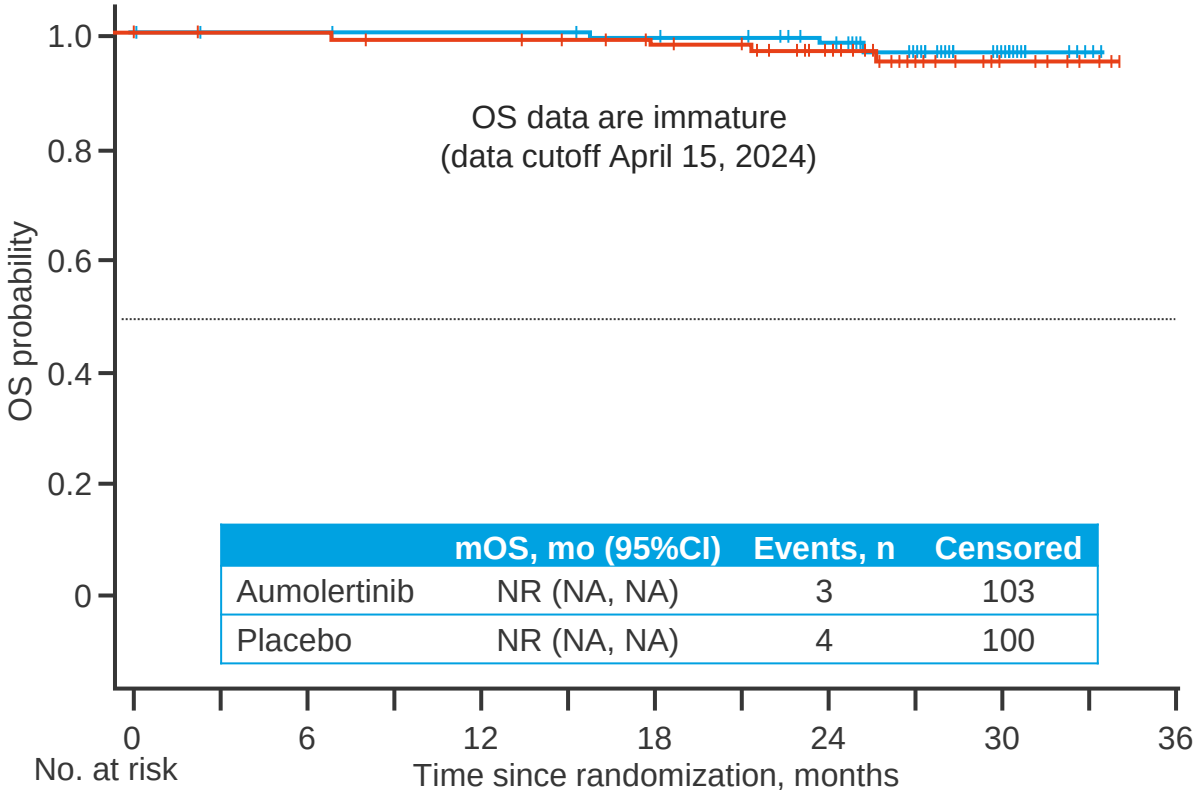
- **Key results**

Disease-free survival



	Events/patients, n	mDFS, mo (95%CI)
Aumolertinib	15/106	NR (29.1, NA)
Placebo	62/104	19.4 (11.2, 26.2)
HR (95%CI); p-value	0.17 (0.09, 0.97); <0.0001	

Overall survival



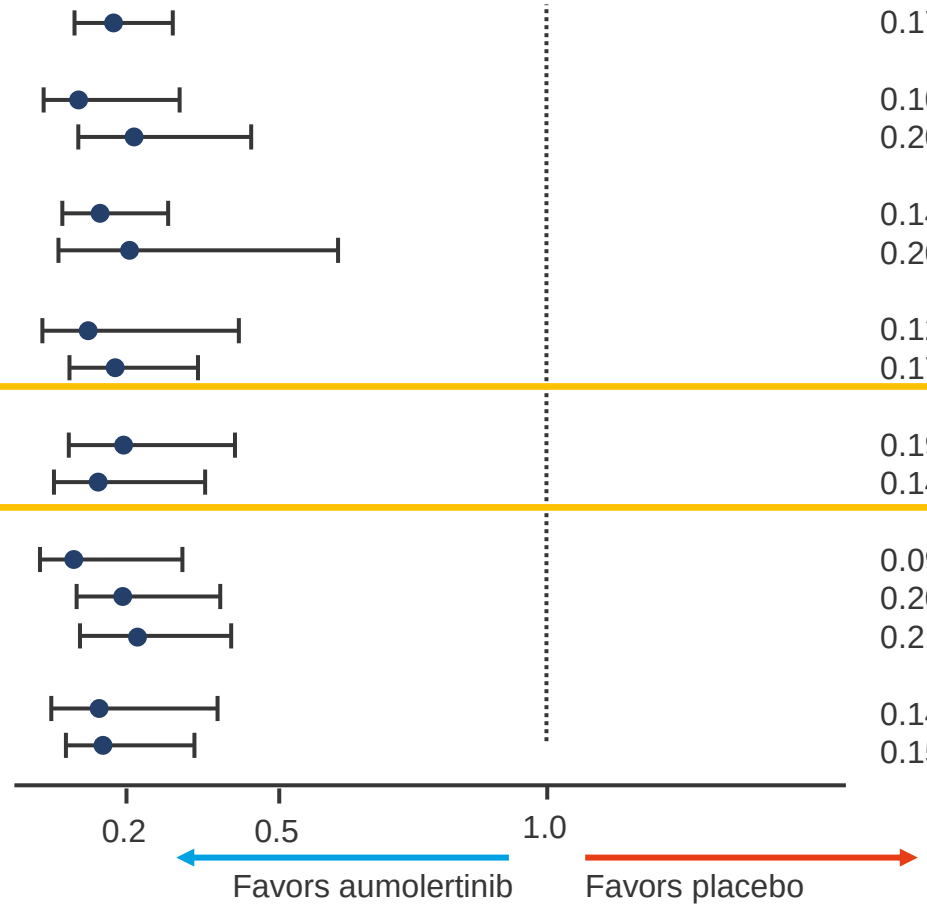
	mOS, mo (95%CI)	Events, n	Censored
Aumolertinib	NR (NA, NA)	3	103
Placebo	NR (NA, NA)	4	100

Four patients with stage I disease were excluded

CT126: Aumolertinib as adjuvant therapy in patients with stage II-IIIB EGFR-mutated NSCLC after complete tumor resection: A randomized, double-blind, placebo-controlled, phase 3 trial (ARTS) – Cheng Y, et al

- **Key results (cont.)**

Subgroup	Aumolertinib Events/patients, n/N	Placebo Events/patients, n/N	HR (95%CI)
mITT set	15/106	62/104	0.17 (0.09, 0.29)
Gender			
Male	4/47	27/44	0.10 (0.04, 0.30)
Female	11/59	36/60	0.20 (0.10, 0.41)
Age, years			
<65	10/76	45/72	0.14 (0.07, 0.28)
≥65	5/30	17/32	0.20 (0.06, 0.60)
Smoking history			
Yes	3/30	21/32	0.12 (0.04, 0.40)
No	12/76	41/72	0.17 (0.09, 0.34)
EGFR mutations			
L858R	9/55	33/52	0.19 (0.09, 0.39)
Ex19del	6/51	29/52	0.14 (0.06, 0.35)
Stage			
II	3/48	24/48	0.09 (0.03, 0.31)
III	12/58	36/56	0.20 (0.10, 0.38)
IIIA/B N2+	12/56	37/55	0.21 (0.11, 0.40)
ECOG PS			
0	6/38	24/41	0.14 (0.05, 0.38)
1	9/68	38/63	0.15 (0.07, 0.32)



Four patients with stage I disease were excluded

Cheng Y, et al. AACR; 2025. Abstract nr CT126

CT126: Aumolertinib as adjuvant therapy in patients with stage II-IIIB EGFR-mutated NSCLC after complete tumor resection: A randomized, double-blind, placebo-controlled, phase 3 trial (ARTS) – Cheng Y, et al

- **Key results (cont.)**

TRAEs, n (%)	Aumolertinib (n=106)	Placebo (n=107)
Any	99 (93.4)	81 (75.7)
Grade ≥3	14 (13.2)	8 (7.5)
Serious	1 (0.9)*	3 (2.8)
Led to dose interruption	8 (7.5)	8 (7.5)
Led to dose reduction	10 (9.4)	2 (1.9)
Led to discontinuation	1 (0.9)*	0

Grade ≥3 TEAEs, n (%)	Aumolertinib (n=106)	Placebo (n=107)
CPK increased	7 (6.6)	0
ALT increased	0	1 (0.9)
COVID-19	0	1 (0.9)
Rash	2 (1.9)	0
Pruritus	1 (0.9)	0
Diarrhea	0	2 (1.9)
Upper respiratory tract infection	1 (0.9)	1 (0.9)

- **Conclusions**
  - In Chinese patients with EGFR-mutated stage II–IIIB NSCLC, aumolertinib demonstrated a significant improvement in DFS post-adjuvant chemotherapy and had a manageable safety profile

*One patient experienced a serious AE (rash) that led to discontinuation

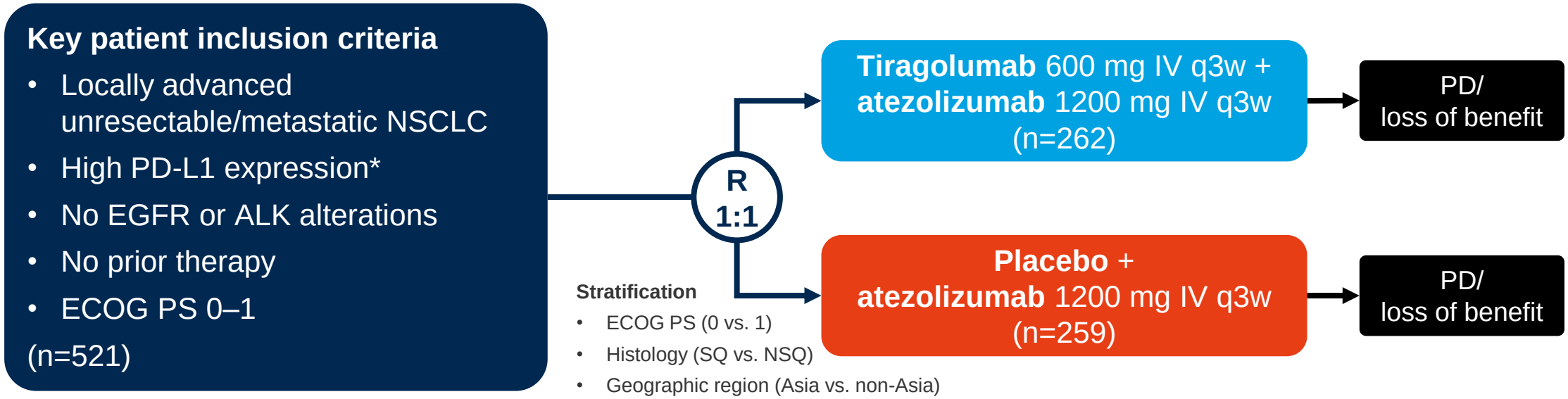
Cheng Y, et al. AACR; 2025. Abstract nr CT126

Advanced NSCLC
Not radically treatable stage III and stage IV

Immunotherapy

CT051: SKYSCRAPER-01: A phase III, randomized trial of tiragolumab (tira) + atezolizumab (atezo) versus placebo (pbo) + atezo in patients (pts) with previously-untreated PD-L1-high, locally advanced unresectable/metastatic NSCLC – Peters S, et al

- **Study objective**
  - To evaluate the efficacy and safety of tiragolumab + atezolizumab in treatment-naïve patients with locally advanced unresectable/metastatic NSCLC and high PD-L1 expression in the phase 3 SKYSCRAPER-01 trial



Primary endpoints

- OS, PFS (investigator) in PAS†

Secondary endpoints

- OS, PFS (investigator) in SAS‡
- ORR, DoR, safety

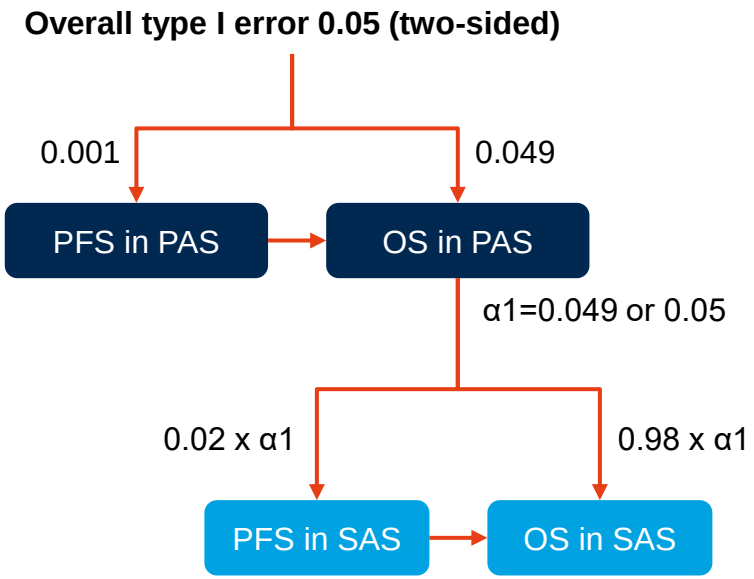
*Centrally assessed using 22C3 pharmDx assay (TPS ≥50%), VENTANA SP263 DCx assay (TC ≥50%), or VENTANA SP142 assay (TC ≥50% or IC ≥10%); †patients with high tumor PD-L1 expression per 22C3 pharmDx assay; ‡patients with high tumor PD-L1 expression per VENTANA SP263 assay

Peters S, et al. AACR; 2025. Abstract nr CT051

CT051: SKYSCRAPER-01: A phase III, randomized trial of tiragolumab (tira) + atezolizumab (atezo) versus placebo (pbo) + atezo in patients (pts) with previously-untreated PD-L1-high, locally advanced unresectable/metastatic NSCLC – Peters S, et al

- **Key results**

	Tiragolumab + atezolizumab	Placebo + atezolizumab	Total
Full analysis set (FAS) High PD-L1 tumor expression per 22C3 (TPS ≥50%), SP263 (TC ≥50%), or SP142 assay (TC ≥50% or IC ≥10%)	266	268	534
Primary analysis set (PAS) High PD-L1 tumor expression per 22C3 assay (TPS ≥50%)	262	259	521
Secondary analysis set (SAS) High PD-L1 tumor expression per SP263 assay (TC ≥50%)	211	209	420
Safety evaluable set All patients who received at least one dose of any treatment	267	263	530



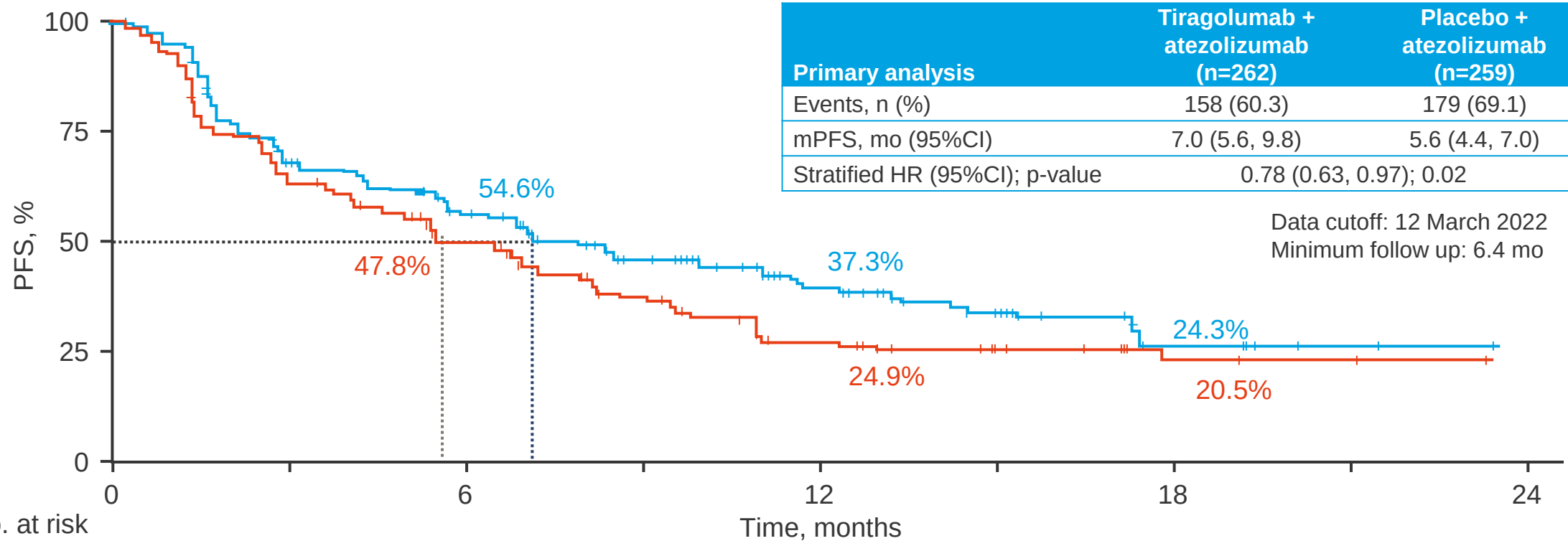
At study initiation PD-L1 testing was by 22C3, enrollment by other assays was permitted from November 2022

Peters S, et al. AACR; 2025. Abstract nr CT051

CT051: SKYSCRAPER-01: A phase III, randomized trial of tiragolumab (tira) + atezolizumab (atezo) versus placebo (pbo) + atezo in patients (pts) with previously-untreated PD-L1-high, locally advanced unresectable/metastatic NSCLC – Peters S, et al

- **Key results (cont.)**

Progression-free survival in PAS



Primary analysis	Tiragolumab + atezolizumab (n=262)	Placebo + atezolizumab (n=259)
Events, n (%)	158 (60.3)	179 (69.1)
mPFS, mo (95%CI)	7.0 (5.6, 9.8)	5.6 (4.4, 7.0)
Stratified HR (95%CI); p-value	0.78 (0.63, 0.97); 0.02	

Data cutoff: 12 March 2022
Minimum follow up: 6.4 mo

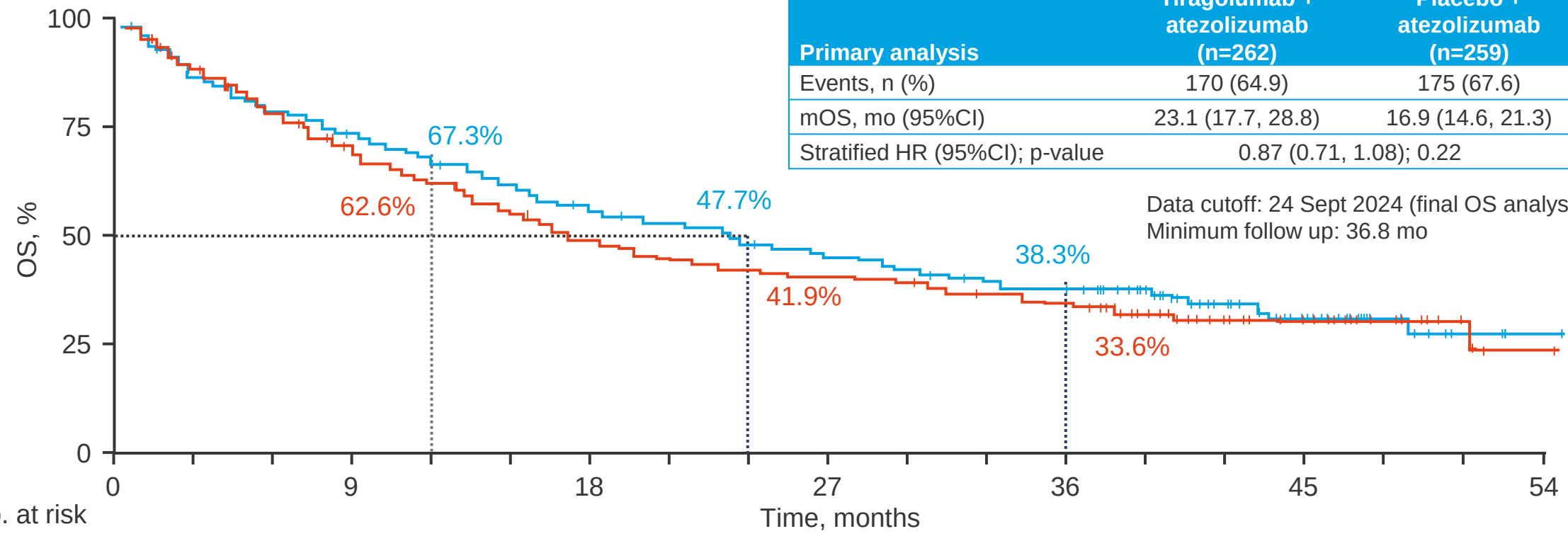
Peters S, et al. AACR; 2025. Abstract nr CT051

CT051: SKYSCRAPER-01: A phase III, randomized trial of tiragolumab (tira) + atezolizumab (atezo) versus placebo (pbo) + atezo in patients (pts) with previously-untreated PD-L1-high, locally advanced unresectable/metastatic NSCLC – Peters S, et al

- **Key results (cont.)**

Overall survival in PAS

Primary analysis	Tiragolumab + atezolizumab (n=262)	Placebo + atezolizumab (n=259)
Events, n (%)	170 (64.9)	175 (67.6)
mOS, mo (95%CI)	23.1 (17.7, 28.8)	16.9 (14.6, 21.3)
Stratified HR (95%CI); p-value	0.87 (0.71, 1.08); 0.22	



CT051: SKYSCRAPER-01: A phase III, randomized trial of tiragolumab (tira) + atezolizumab (atezo) versus placebo (pbo) + atezo in patients (pts) with previously-untreated PD-L1-high, locally advanced unresectable/metastatic NSCLC – Peters S, et al

- **Key results (cont.)**

SAS population	Tiragolumab + atezolizumab (n=211)	Placebo + atezolizumab (n=209)
PFS		
Events, n (%)	172 (81.5)	178 (85.2)
mPFS, mo (95%CI)	8.3 (6.2, 11.3)	5.7 (4.7, 7.3)
Stratified HR (95%CI)	0.86 (0.69, 1.06)	
OS		
Events, n (%)	131 (62.1)	135 (64.6)
mOS, mo (95%CI)	24.6 (17.9, 32.0)	20.6 (16.6, 29.3)
Stratified HR (95%CI)	0.93 (0.73, 1.18)	

PAS population	Tiragolumab + atezolizumab (n=262)	Placebo + atezolizumab (n=259)
ORR, % (95%CI)	45.8 (39.7, 52.0)	35.1 (29.4, 41.3)
BOR, %		
CR	1.5	1.2
PR	44.3	34.0
SD	22.1	27.4
PD	24.4	26.3
mDoR, mo (95%CI)	18.0 (13.6, 24.4)	14.6 (9.7, 18.6)

AEs, n (%)	Tiragolumab + atezolizumab (n=262)	Placebo + atezolizumab (n=259)
Any	256 (95.9)	240 (91.3)
Grade 3–4	110 (41.2)	89 (33.8)
Grade 5	29 (10.9)	26 (9.9)
TRAE	202 (75.7)	158 (60.1)
Grade 3–4	53 (19.9)	25 (9.5)
Grade 5	4 (1.5)	2 (0.8)
SAE	115 (43.1)	108 (41.1)
Led to discontinuation	43 (16.1)	17 (6.5)
irAE	187 (70.0)	133 (50.6)
Grade 3–4	43 (16.1)	26 (9.9)
Grade 5	2 (0.7)	2 (0.8)
Corticosteroids	65 (24.3)	33 (12.5)

- **Conclusions**
  - In previously untreated patients with locally advanced unresectable/metastatic NSCLC and high PD-L1 expression, tiragolumab + atezolizumab did not provide any additional benefit over atezolizumab alone and had an acceptable safety profile

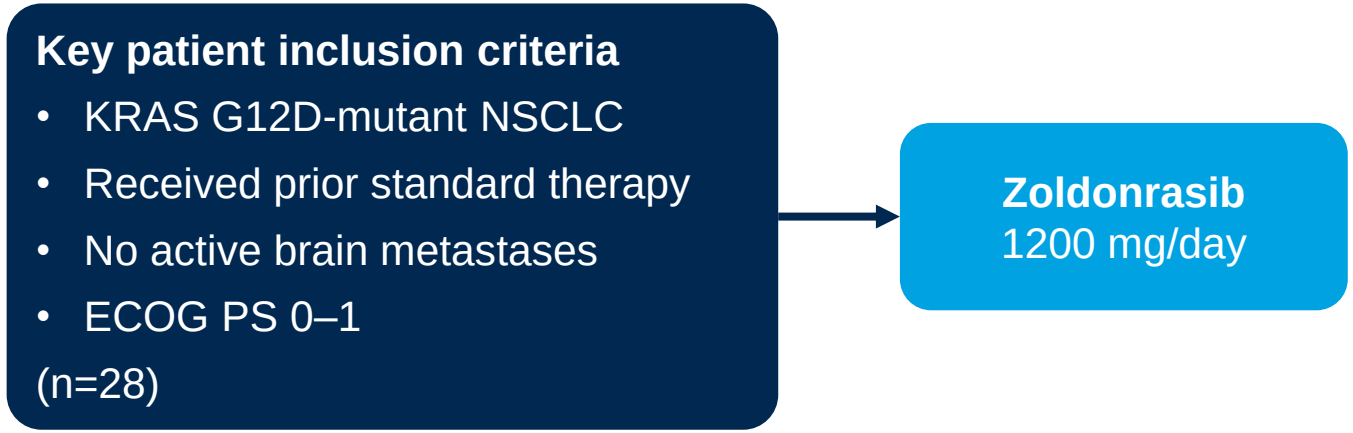
Peters S, et al. AACR; 2025. Abstract nr CT051

Advanced NSCLC
Not radically treatable stage III and stage IV

Targeted therapies

CT019: Preliminary safety and antitumor activity of zoldonrasib (RMC-9805), an oral, RAS(ON) G12D-selective, tri-complex inhibitor in patients with KRAS G12D NSCLC from a phase 1 study in advanced solid tumors – Arbour KC, et al

- **Study objective**
  - To evaluate the preliminary antitumor activity and safety of zoldonrasib, a RAS G12D inhibitor, in a cohort of patients with KRAS G12D-mutant NSCLC in the dose expansion and optimization portion of a phase 1 study

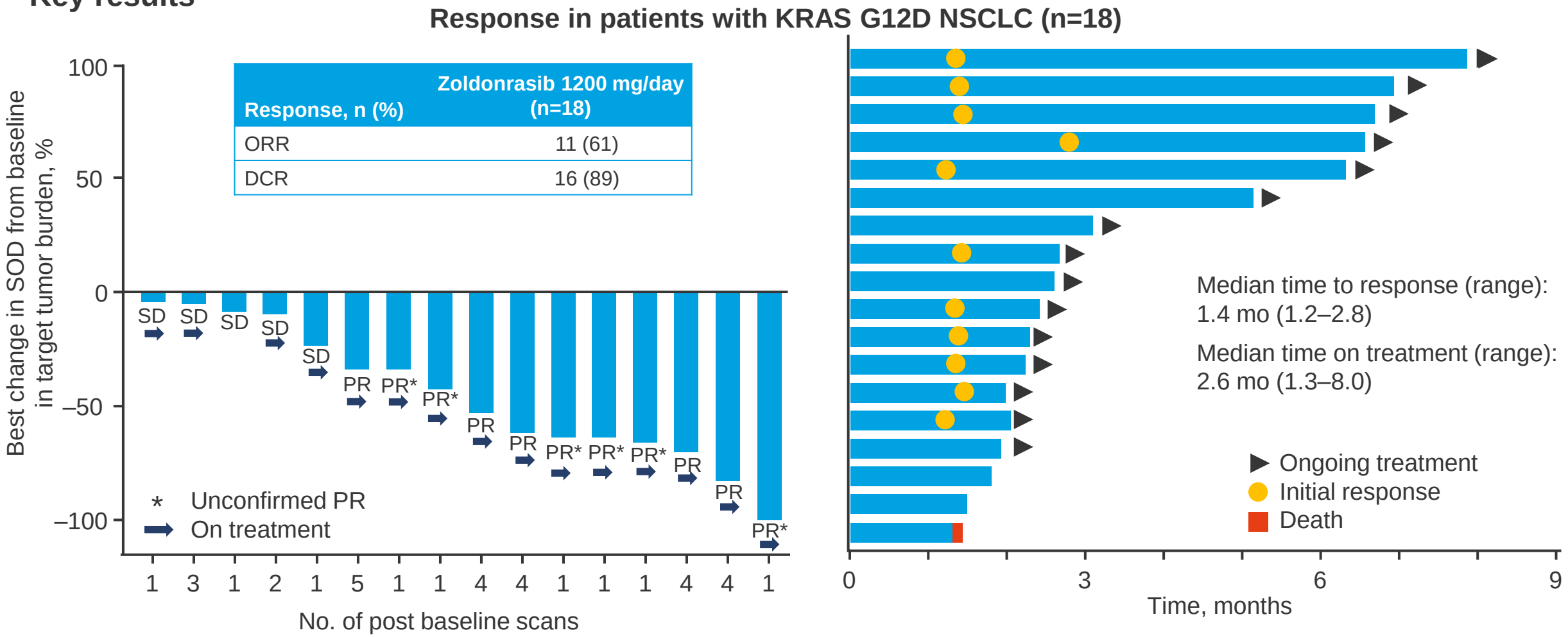


Endpoints

- Safety, PK, antitumor activity

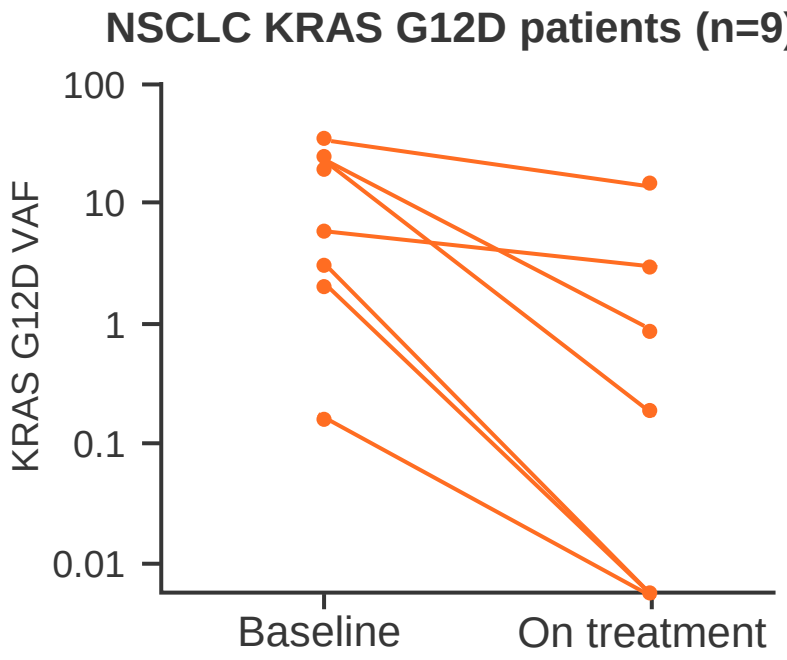
CT019: Preliminary safety and antitumor activity of zoldonrasib (RMC-9805), an oral, RAS(ON) G12D-selective, tri-complex inhibitor in patients with KRAS G12D NSCLC from a phase 1 study in advanced solid tumors – Arbour KC, et al

- **Key results**



CT019: Preliminary safety and antitumor activity of zoldonrasib (RMC-9805), an oral, RAS(ON) G12D-selective, tri-complex inhibitor in patients with KRAS G12D NSCLC from a phase 1 study in advanced solid tumors – Arbour KC, et al

- **Key results (cont.)**



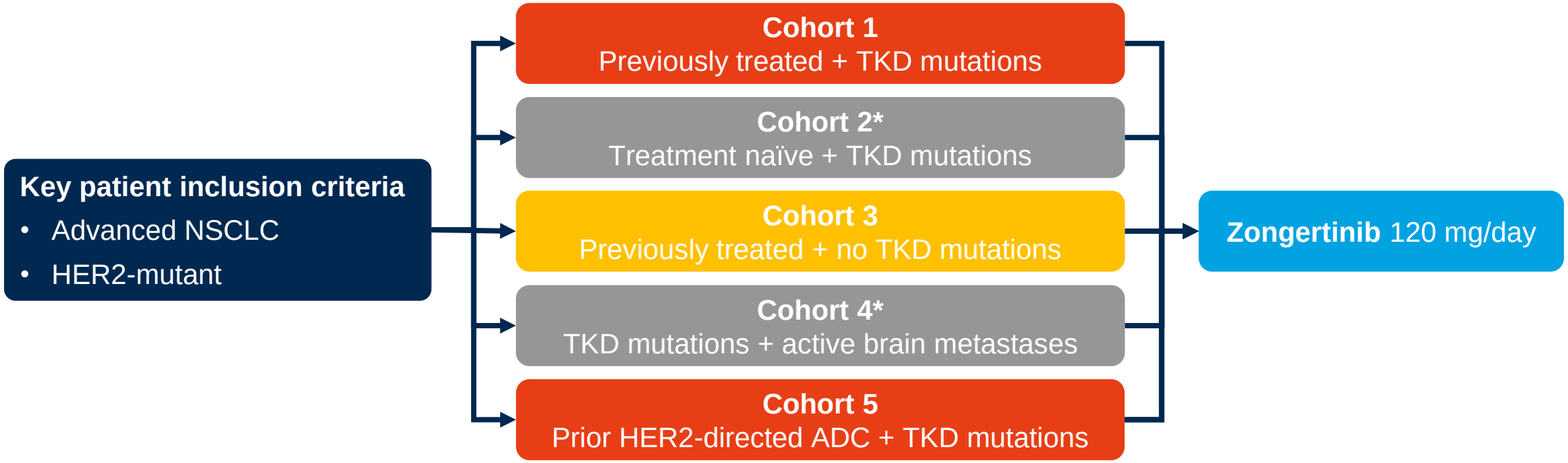
TRAEs in all patients*, n (%)	Zoldonrasib 1200 mg/day (n=90)
Any	67 (74)
Occurring in ≥10% of patients	
Nausea	35 (39)
Diarrhea	22 (24)
Vomiting	16 (18)
Rash	11 (12)
Other select	
AST increased	7 (8)
ALT increased	6 (7)
Stomatitis/mucositis	1 (1)
Led to dose interruption	8 (9)
Led to dose reduction	4 (4)
Led to discontinuation	1 (1)

- **Conclusions**
  - In patients with KRAS G12D-mutant NSCLC, zoldonrasib demonstrated preliminary promising antitumor activity with a manageable safety profile

*PDAC and NSCLC

CT050: Zongertinib in patients with pretreated HER2-mutant advanced NSCLC: Beamion LUNG-1 – Heymach JV, et al

- **Study objective**
  - To evaluate the preliminary efficacy and safety of zongertinib in previously treated patients with HER2-mutant NSCLC in the phase 1 Beamion LUNG-1 trial



Primary endpoint

- Cohort 1 and 5: ORR (BICR, RECIST v1.1)
- Cohort 3: ORR (investigator)

Secondary endpoints

- DoR, DCR, PFS, safety

*Analysis ongoing – no data available yet

Heymach JV, et al. AACR; 2025. Abstract nr CT050

CT050: Zongertinib in patients with pretreated HER2-mutant advanced NSCLC: Beamion LUNG-1 – Heymach JV, et al

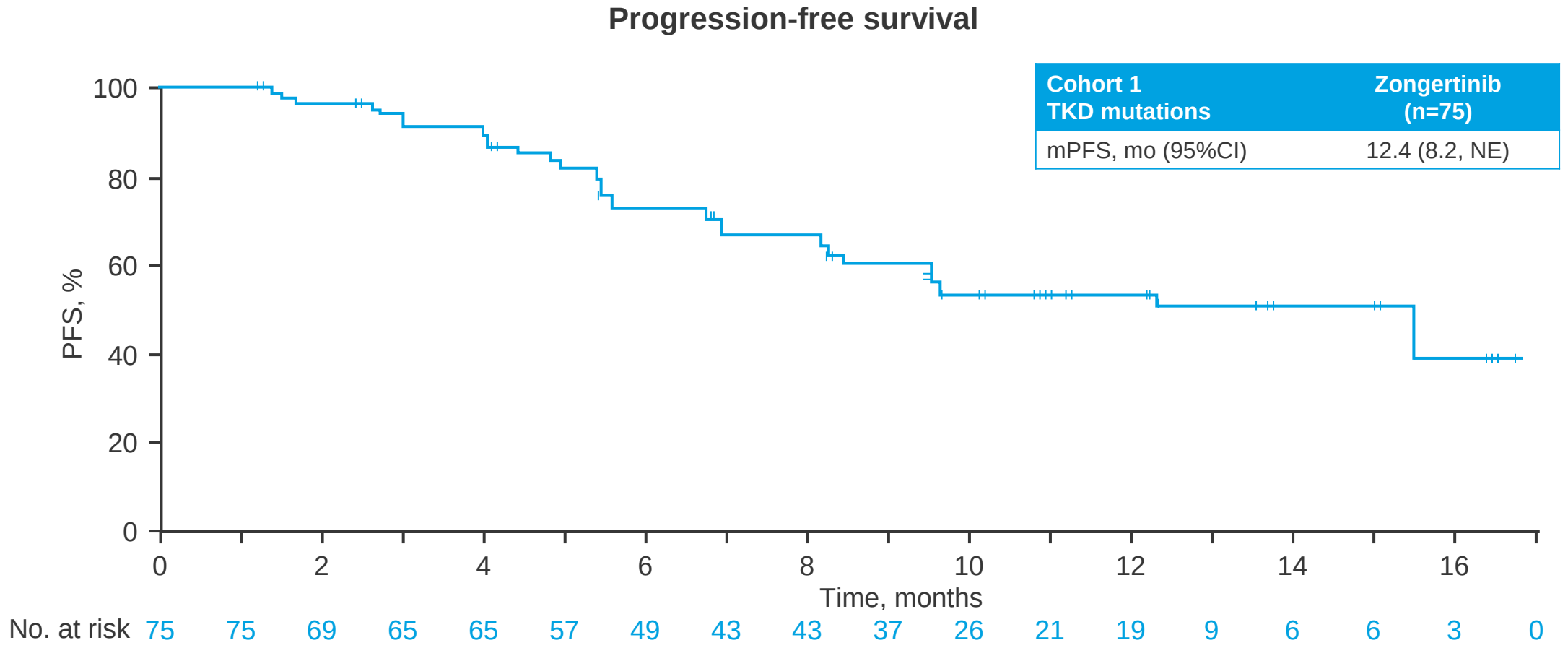
- **Key results**

Responses	Cohort 1 TKD mutations (n=75)	Cohort 5 Prior HER2-directed ADC + TDK mutations (n=31)	Cohort 3 No TKD mutations (n=20)
ORR, % (95%CI)	71 (60, 80)	48 (32, 65)	30 (15, 52)
BOR, %			
CR	7	3	0
PR	64	45	30
SD	25	48	35
PD	4	0	30
NE	0	3	5
DCR, % (95%CI)	96 (89, 99)	97 (84, 99)	65 (43, 82)
mDoR, mo (95%CI)	14.1 (6.9, NE)	-	-
Intracranial response			
ORR, % (95%CI)	41 (25, 59)	-	-
BOR, %			
CR	15	-	-
PR	26	-	-
SD	41	-	-
PD	7	-	-
NE	11	-	-
DCR, % (95%CI)	81 (63, 92)	-	-

Heymach JV, et al. AACR; 2025. Abstract nr CT050

CT050: Zongertinib in patients with pretreated HER2-mutant advanced NSCLC: Beamion LUNG-1 – Heymach JV, et al

- **Key results (cont.)**



Heymach JV, et al. AACR; 2025. Abstract nr CT050

CT050: Zongertinib in patients with pretreated HER2-mutant advanced NSCLC: Beamion LUNG-1 – Heymach JV, et al

- **Key results (cont.)**

TRAEs in Cohort 1, n (%)	All grades	Grade ≥3
Any	73 (97)	13 (17)
Diarrhea	42 (56)	1 (1)
Rash	25 (33)	0
AST increased	18 (24)	4 (5)
ALT increased	16 (21)	6 (8)
Nausea	11 (15)	0
Dry skin	11 (15)	0
Pruritus	10 (13)	0
WBC count decreased	10 (13)	0
Anemia	9 (12)	0
Neutrophil count decreased	9 (12)	1 (1)
Nail disorder	8 (11)	0
Led to dose reduction	5 (7)	
Led to discontinuation	2 (3)	

- **Conclusions**
  - In previously treated patients with HER2-mutant advanced NSCLC, zongertinib demonstrated preliminary encouraging antitumor activity with a manageable safety profile

Heymach JV, et al. AACR; 2025. Abstract nr CT050

CT052: A highly selective, brain-penetrant and overcoming G2032R resistance ROS1 inhibitor JYP0322 in NSCLC patients with ROS1 fusion – Zhao H, et al

- **Study objective**
  - To evaluate the preliminary efficacy and safety of JYP0322, a ROS1 inhibitor, in patients with NSCLC and a ROS1 fusion in a phase 1 study in a Chinese population

Key patient inclusion criteria
- NSCLC
- ROS1 fusion
- ROS1 TKI naïve or pretreated
- Stable CNS metastases
- ECOG PS 0–1

Dose escalation

JYP0322
50, 100, 200 mg/day
100, 150, 200 mg bid
150 mg tid
(n=20)

Dose expansion

JYP0322
100 mg bid
150 mg bid
150 mg tid
(n=61, ongoing)

Primary endpoints
- MTD, RP2D

Secondary endpoints
- Safety, PK, preliminary antitumor activity, intracranial activity

Zhao H, et al. AACR; 2025. Abstract nr CT052

CT052: A highly selective, brain-penetrant and overcoming G2032R resistance ROS1 inhibitor JYP0322 in NSCLC patients with ROS1 fusion – Zhao H, et al

- **Key results**

Responses in evaluable patients (n=66)	ROS1 TKI naïve (n=19)	ROS1 TKI pretreated (± chemotherapy) All (n=47)	1 ROS1 TKI (n=22)	≥2 ROS1 TKIs (n=20)	Prior lorlatinib, taletrectinib or repotrectinib (n=9)	G2032R co-mutation (n=7)
ORR, n (%)	15 (78.9)	27 (57.4)	11 (50.0)	12 (60.0)	4 (44.4)	6 (85.7)
DCR, n (%)	16 (84.2)	35 (74.5)	17 (77.3)	14 (70.0)	5 (55.6)	-

Intracranial responses in patients with brain metastases	
ORR, n/N (%)	3/7 (42.9)
DCR, n/N (%)	25/34 (73.5)

Zhao H, et al. AACR; 2025. Abstract nr CT052

CT052: A highly selective, brain-penetrant and overcoming G2032R resistance ROS1 inhibitor JYP0322 in NSCLC patients with ROS1 fusion – Zhao H, et al

- **Key results (cont.)**

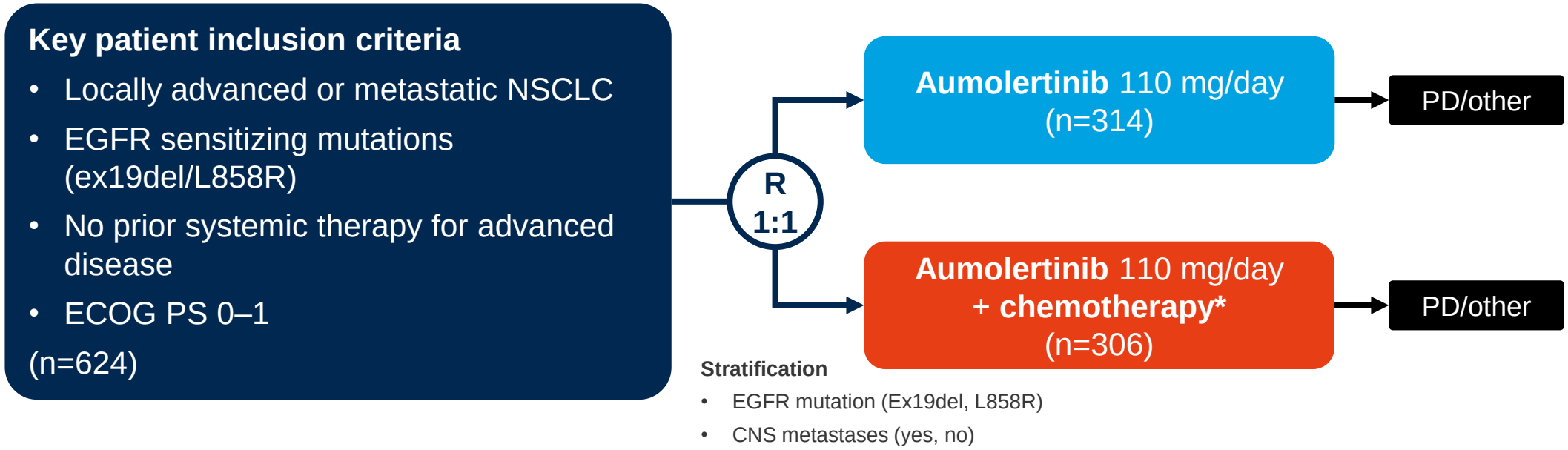
TRAEs, n (%)	JYP0322 (n=81)
Any	73 (90.1)
Grade ≥3	13 (16.0)
Serious	9 (11.1)
Led to dose interruption	13 (16.0)
Led to dose reduction	2 (2.5)
Led to discontinuation	4 (4.9)

Grade ≥3 TRAEs, n (%)	JYP0322 (n=81)
Weight increased	5 (6.2)
Cholesterol increased	1 (1.2)
Rash	1 (1.2)

- **Conclusions**
  - In Chinese patients with ROS1 fusion-positive NSCLC, JYP0322 demonstrated preliminary clinical activity in those who were ROS1 TKI naïve or pretreated with an acceptable safety profile

CT053: Aumolertinib with or without chemotherapy as first line treatment in locally advanced or metastatic NSCLC with sensitizing EGFR mutations (AENEAS2) – Lu S, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L aumolertinib ± chemotherapy in patients with locally advanced or metastatic NSCLC and EGFR sensitizing mutations in the phase 3 AENEAS2 trial in a Chinese population



Primary endpoint

- PFS (BICR)

Secondary endpoints

- PFS (investigator), ORR, DCR, DoR, OS, safety

*Pemetrexed 500 mg/m^2 + cisplatin 75 mg/m^2 or carboplatin AUC5 q3w for 4–6 cycles followed by pemetrexed 500 mg/m^2 q3w

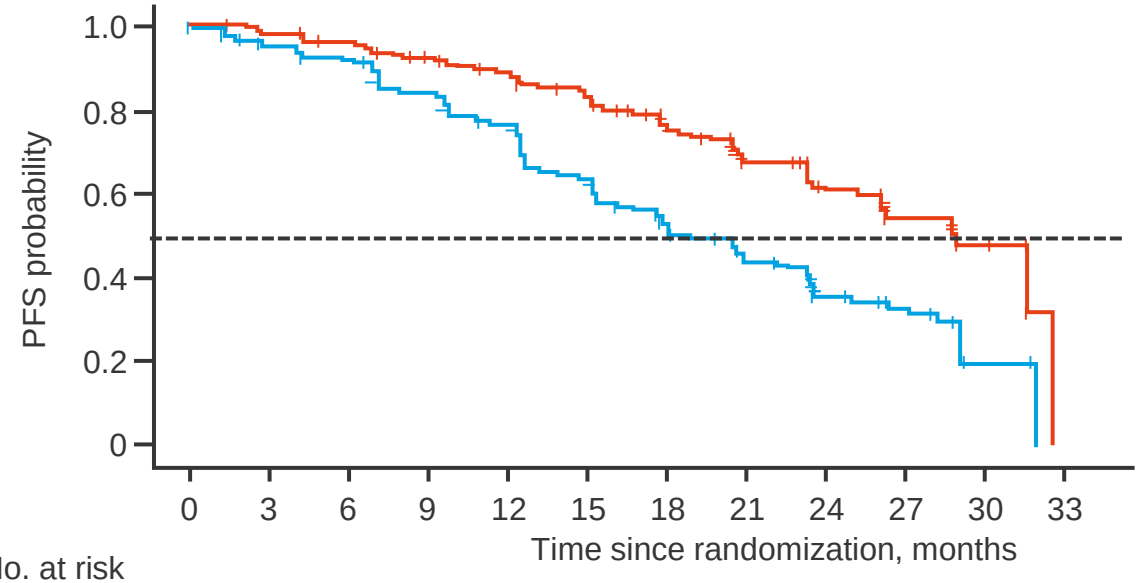
Lu S, et al. AACR; 2025. Abstract nr CT053

CT053: Aumolertinib with or without chemotherapy as first line treatment in locally advanced or metastatic NSCLC with sensitizing EGFR mutations (AENEAS2) – Lu S, et al

- **Key results**

Progression-free survival

	Aumolertinib + CTx	Aumolertinib alone
mPFS, mo (95%CI)	28.9 (26.3, NA)	18.9 (17.8, 21.1)
HR (95% CI); Log-rank p-value	0.47 (0.37, 0.60); <0.0001	



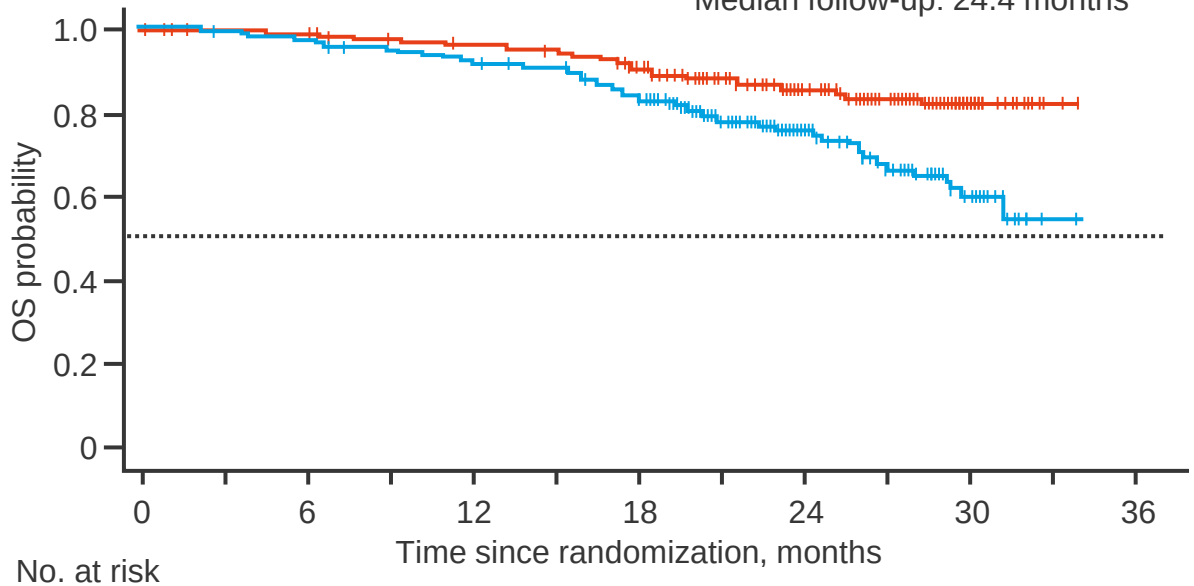
No. at risk

Aumolertinib + CTx	310	288	279	266	254	238	192	122	76	40	10	0
Aumolertinib	314	293	275	248	223	183	126	77	46	26	3	0

Overall survival

	Aumolertinib + CTx	Aumolertinib alone
mOS, mo	NR	NR
HR (95% CI)	0.44 (0.31, 0.64)	

Median follow-up: 24.4 months



No. at risk

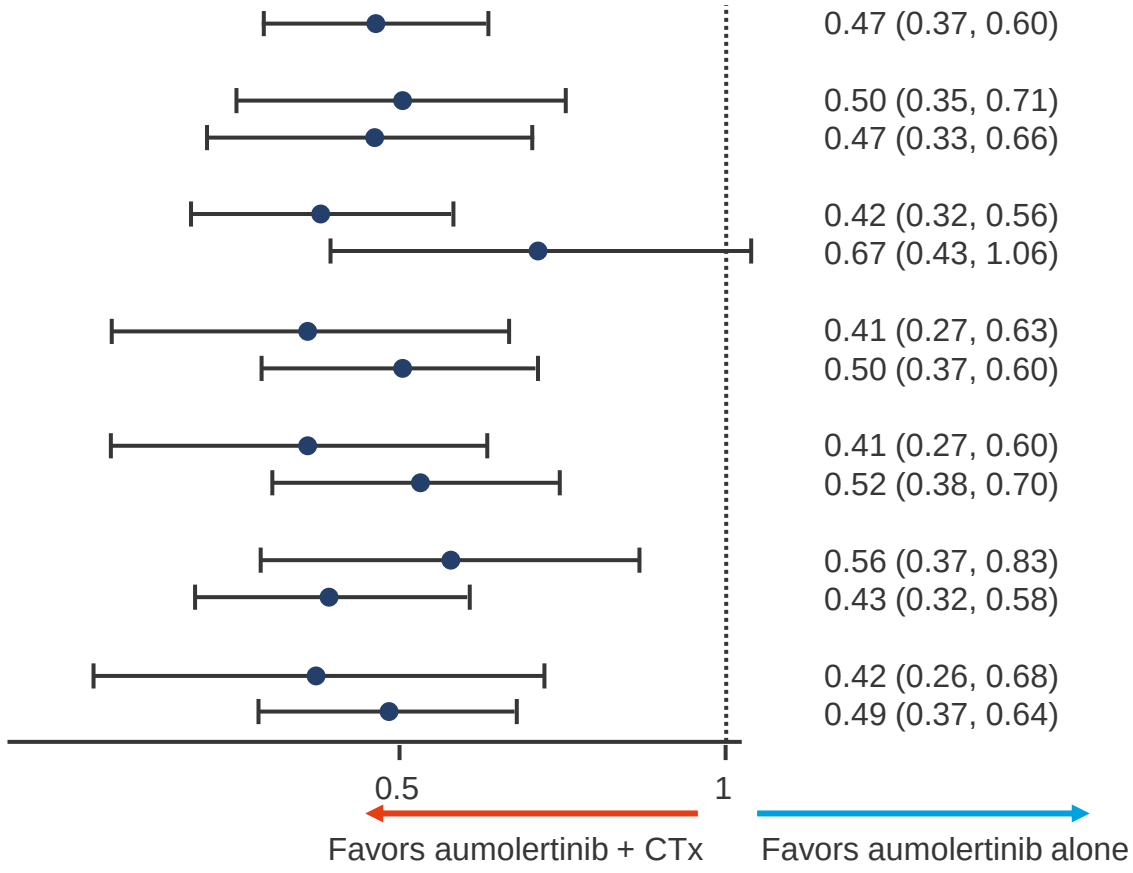
Aumolertinib + CTx	310	301	299	292	288	283	268	211	141	101	37	2	0
Aumolertinib	314	309	302	294	284	277	251	183	120	80	27	1	0

Lu S, et al. AACR; 2025. Abstract nr CT053

CT053: Aumolertinib with or without chemotherapy as first line treatment in locally advanced or metastatic NSCLC with sensitizing EGFR mutations (AENEAS2) – Lu S, et al

- **Key results (cont.)**

Subgroup	Events, n: Aumolertinib + CTx	Events, n: Aumolertinib alone	mPFS, mo: Aumolertinib + CTx	mPFS, mo: Aumolertinib alone	HR (95%CI)
FAS	111/310	179/314	28.9	18.9	0.47 (0.37, 0.60)
Gender					
Male	52/138	90/149	28.7	17.9	0.50 (0.35, 0.71)
Female	59/172	89/165	31.7	20.7	0.47 (0.33, 0.66)
Age					
<65 years	75/216	137/227	31.7	18.1	0.42 (0.32, 0.56)
≥65 years	36/94	42/87	26.3	23.7	0.67 (0.43, 1.06)
Smoking history					
Yes	36/87	59/92	26.3	15.2	0.41 (0.27, 0.63)
No	75/223	120/222	31.7	20.8	0.50 (0.37, 0.60)
EGFR mutations					
Ex19del	38/152	77/154	NR	23.5	0.41 (0.27, 0.60)
L858R	73/158	102/160	23.6	17.8	0.52 (0.38, 0.70)
Baseline CNS metastases					
Yes	41/93	62/97	26.3	18.0	0.56 (0.37, 0.83)
No	70/217	117/217	31.7	20.5	0.43 (0.32, 0.58)
Baseline ECOG PS					
0	29/86	52/88	31.7	18.0	0.42 (0.26, 0.68)
1	82/224	127/226	28.8	20.5	0.49 (0.37, 0.64)



Lu S, et al. AACR; 2025. Abstract nr CT053

CT053: Aumolertinib with or without chemotherapy as first line treatment in locally advanced or metastatic NSCLC with sensitizing EGFR mutations (AENEAS2) – Lu S, et al

- **Key results (cont.)**

Response	Aumolertinib + CTx (n=310)	Aumolertinib alone (n=314)
ORR, % (95%CI)	93.2 (89.8, 95.8)	87.3 (83.1, 90.7)
BOR, %		
PR	93.2	87.3
SD	3.2	9.2
PD	0	2.5
DCR, % (95%CI)	96.5 (93.7, 98.2)	96.5 (93.8, 98.2)
mDoR, mo (95%CI)	27.6 (24.8, NA)	19.3 (16.6, 22.0)

AEs, n (%)	Aumolertinib + CTx (n=304)	Aumolertinib alone (n=316)
Any	304 (100)	298 (94.3)
Grade ≥3	242 (79.6)	110 (34.8)
Serious	109 (35.9)	53 (16.8)
Led to dose interruption	195 (64.1)	79 (25.0)
Led to dose reduction	133 (43.8)	11 (3.5)
Led to discontinuation	64 (21.1)	5 (1.6)
Led to death	4 (1.3)	8 (2.5)

- **Conclusions**
  - In Chinese patients with locally advanced or metastatic EGFR-mutant NSCLC, 1L aumolertinib + chemotherapy demonstrated a significant improvement in PFS over aumolertinib alone

3779: LY4050784, a selective inhibitor of SMARCA2, demonstrates synergistic activity in combinations with pembrolizumab or KRAS inhibitors – Brooks NA, et al

- **Study objective**
  - To evaluate the in vivo and in vitro activity of LY4050784, a selective SMARC2 inhibitor, combined with chemotherapies, pembrolizumab, and KRAS inhibitors in preclinical SMARCA4-mutant human cancer models

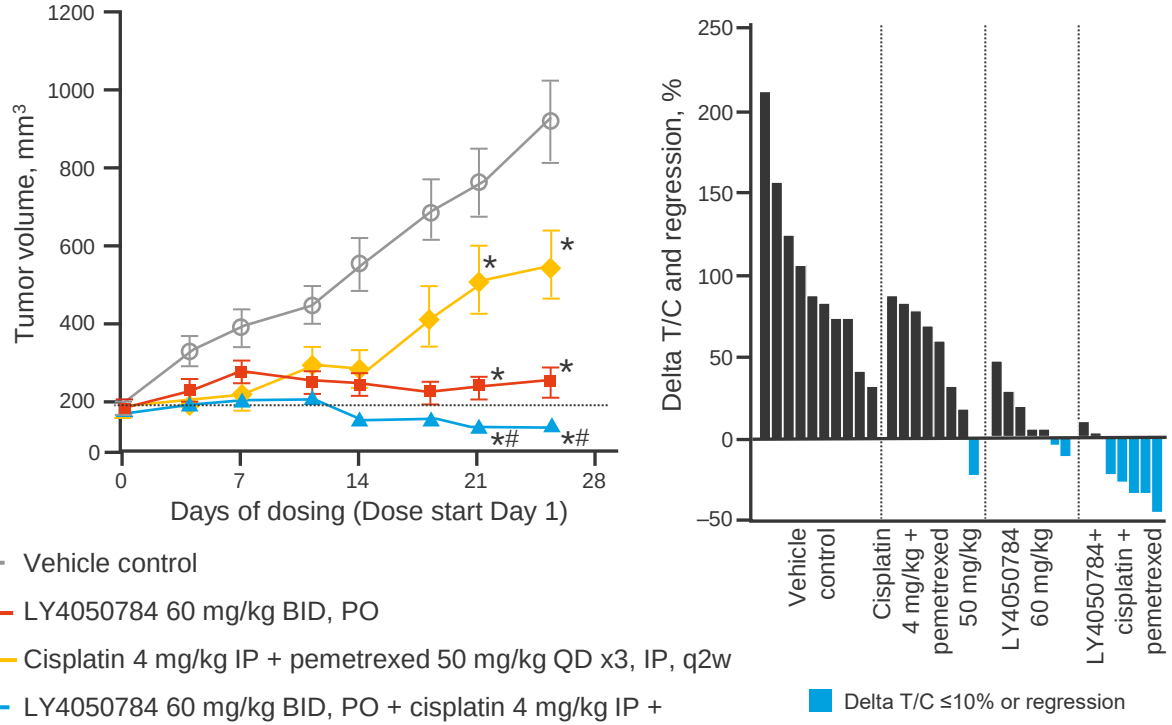
- **Methods**
  - LY4050784 in combined with chemotherapies (paclitaxel, cisplatin, and pemetrexed), pembrolizumab, and KRAS inhibitors was assessed in vitro and in vivo using preclinical SMARCA4-mutant human cancer models
  - LY4050784 combined with pembrolizumab was evaluated in a humanized KRAS- and SMARCA4-mutant lung cancer xenograft model
  - LY4050784 combined with both mutant-selective KRAS G12C and G12D inhibitors (olomorasib and LY3962673, respectively) and the isoform-selective pan-KRAS inhibitor LY4066434 was assessed in SMARCA4 and KRAS co-mutated lung, pancreatic, and colon cancer models

Brooks NA, et al. AACR; 2025. Abstract nr 3779

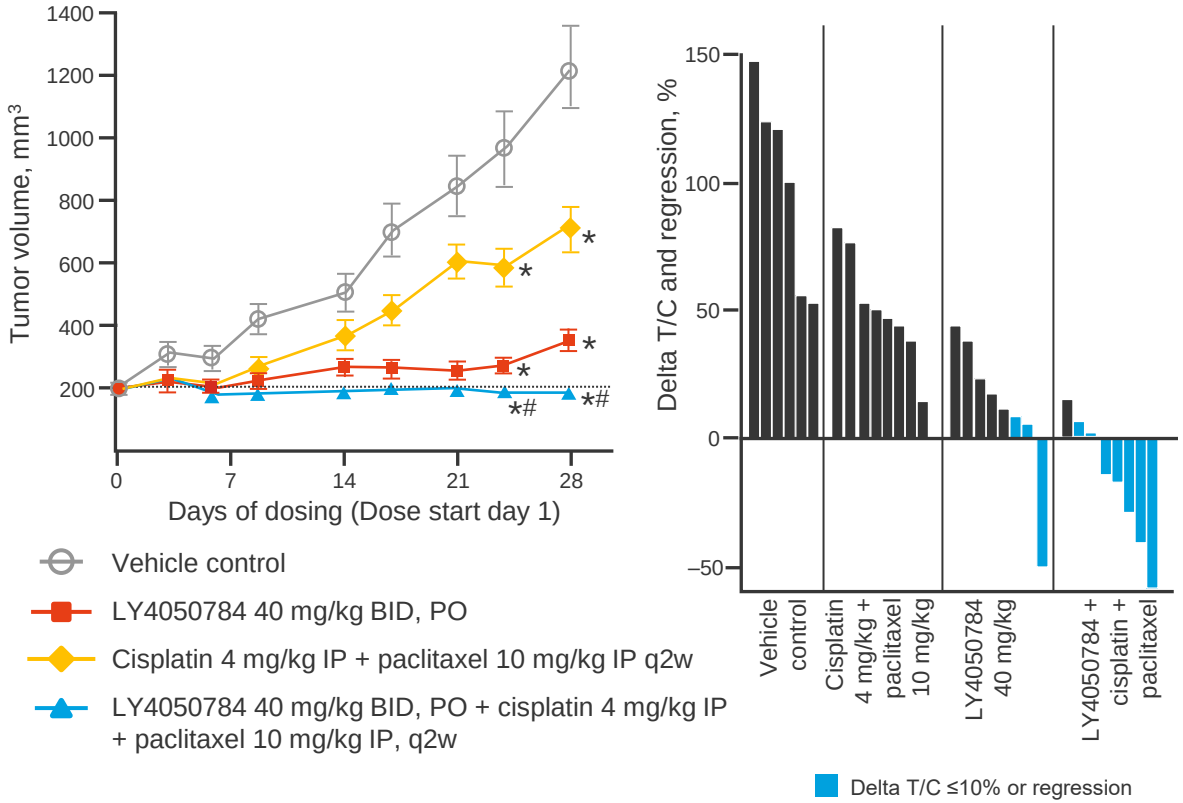
3779: LY4050784, a selective inhibitor of SMARCA2, demonstrates synergistic activity in combinations with pembrolizumab or KRAS inhibitors – Brooks NA, et al

- **Key results**

A549 xenograft model, nude mice
LY4050784 + cisplatin + pemetrexed



RERF-LC-AI xenograft model, nude mice
LY4050784 + cisplatin + paclitaxel



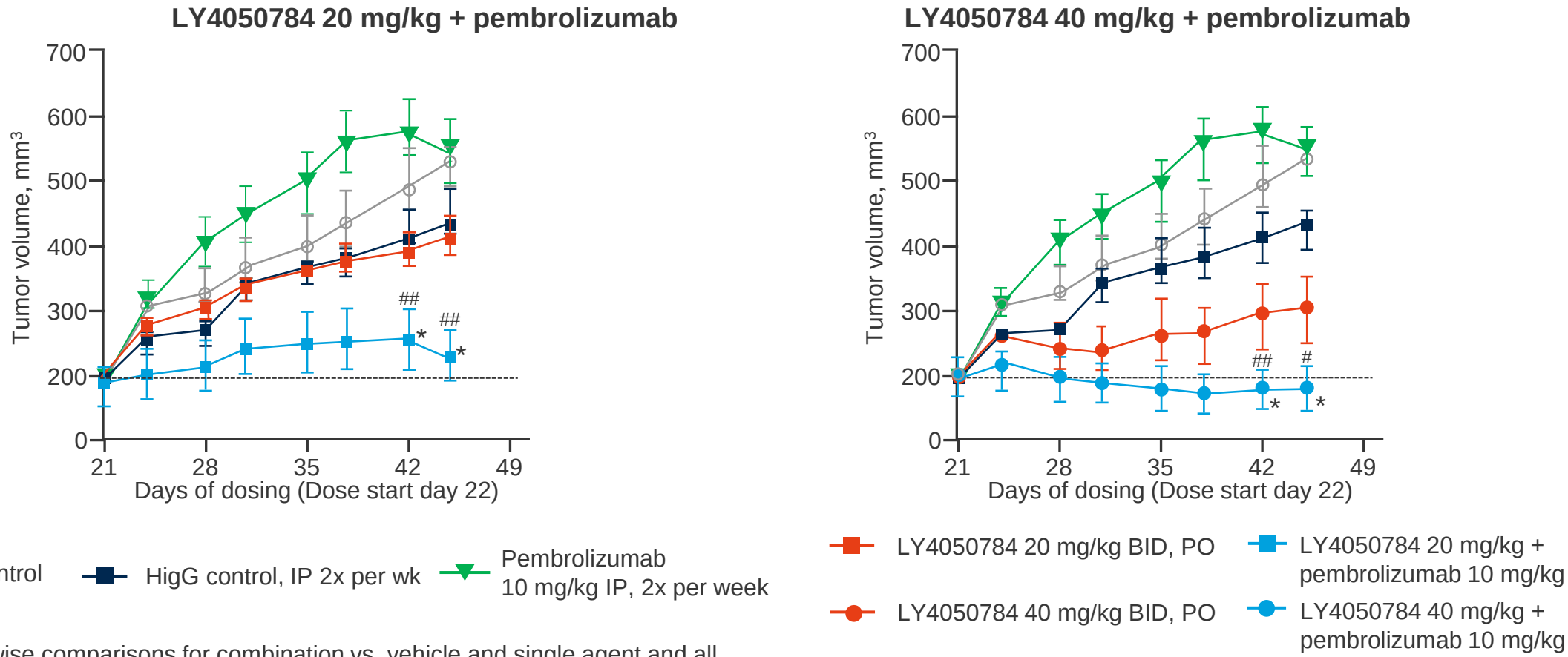
*p≤0.05 for pairwise comparisons for combination vs. vehicle and single agent and all treatment groups vs. vehicle; #additive by Bliss independence analysis

3779: LY4050784, a selective inhibitor of SMARCA2, demonstrates synergistic activity in combinations with pembrolizumab or KRAS inhibitors – Brooks NA, et al

- **Key results (cont.)**

A549 xenograft (CD34+ HSC humanized model)

SMARCA4 Q729fs/H736Y, KRAS G12S, STK11 Q37A, KEAP1 G333C, ATR splice



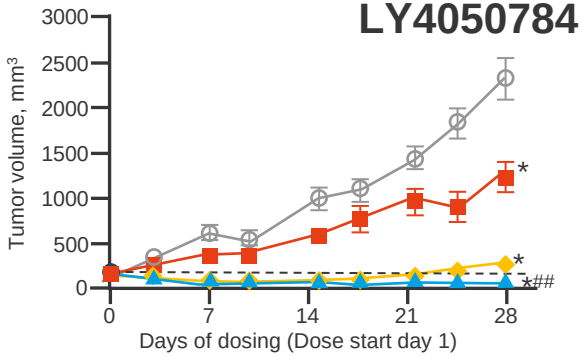
*p≤0.05 for pairwise comparisons for combination vs. vehicle and single agent and all treatment groups vs. vehicle; #additive, ##synergistic by Bliss independence analysis

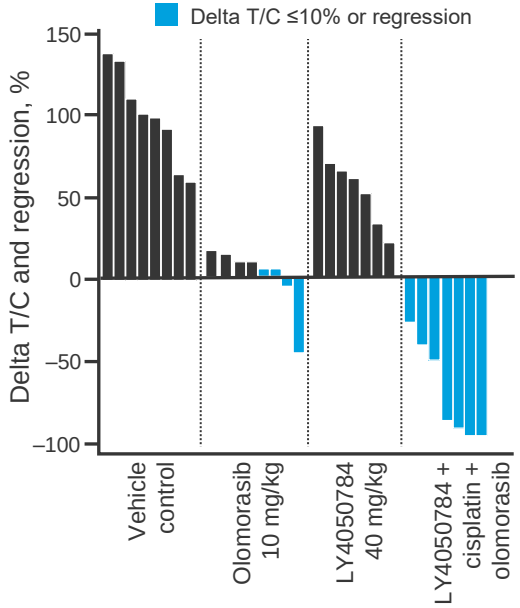
Brooks NA, et al. AACR; 2025. Abstract nr 3779

3779: LY4050784, a selective inhibitor of SMARCA2, demonstrates synergistic activity in combinations with pembrolizumab or KRAS inhibitors – Brooks NA, et al

- **Key results (cont.)**

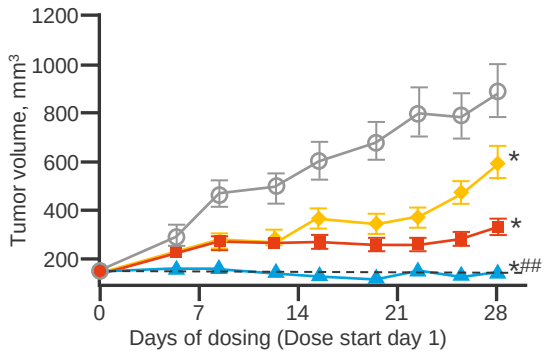
NCI-H2030 xenograft, NSG mice
LY4050784 + olomorasib

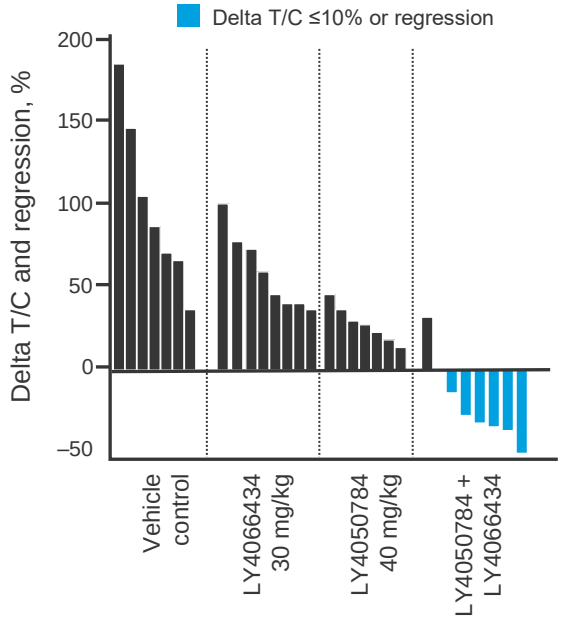




- Vehicle control
- LY4050784 60 mg/kg BID, PO
- Cisplatin 4 mg/kg IP + pemetrexed 50 mg/kg QD x3, IP, q2w
- LY4050784 60 mg/kg BID, PO + cisplatin 4 mg/kg IP + pemetrexed 50 mg/kg QD x3, IP, q2w

A459 xenograft study, nude mice





- Vehicle control
- LY4050784 40 mg/kg BID, PO
- LY4066434 30 mg/kg BID, PO
- LY4050784 40 mg/kg BID, PO + LY4066434 30 mg/kg BID, PO

- **Conclusions**
  - LY4050784 combined with standard of care chemotherapies, pembrolizumab and KRAS inhibitors showed synergistic activity in various in vitro and in vivo models

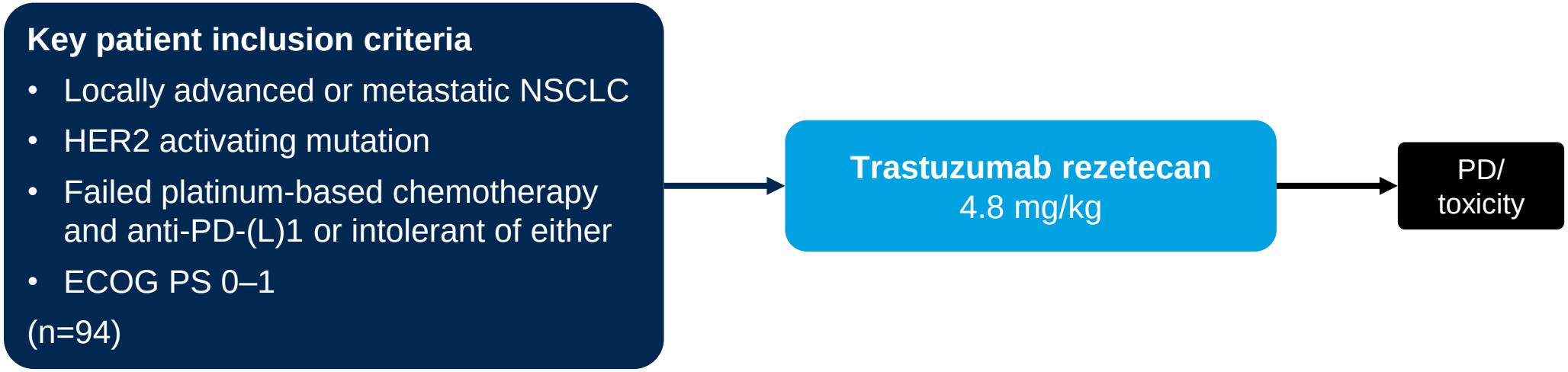
*p≤0.05 for pairwise comparisons for combination vs. vehicle and single agent and all treatment groups vs. vehicle; ##synergistic (p<0.05) by Bliss independence analysis

Advanced NSCLC
Not radically treatable stage III and stage IV

ADC and other therapies

CT009: SHR-A1811, a HER2-directed antibody-drug conjugate (ADC), in advanced HER2-mutant non-small cell lung cancer (NSCLC): Updated phase 2 results from HORIZON-Lung – Lu S, et al

- **Study objective**
  - To evaluate the efficacy and safety of trastuzumab rezetecan (SHR-A1811, a HER2-directed ADC), in patients with HER2-mutant NSCLC in the phase 2 portion of the HORIZON-Lung trial in a Chinese population



Primary endpoint

- ORR (IRC)

Secondary endpoints

- ORR (investigator), DCR, DoR, PFS, OS, safety

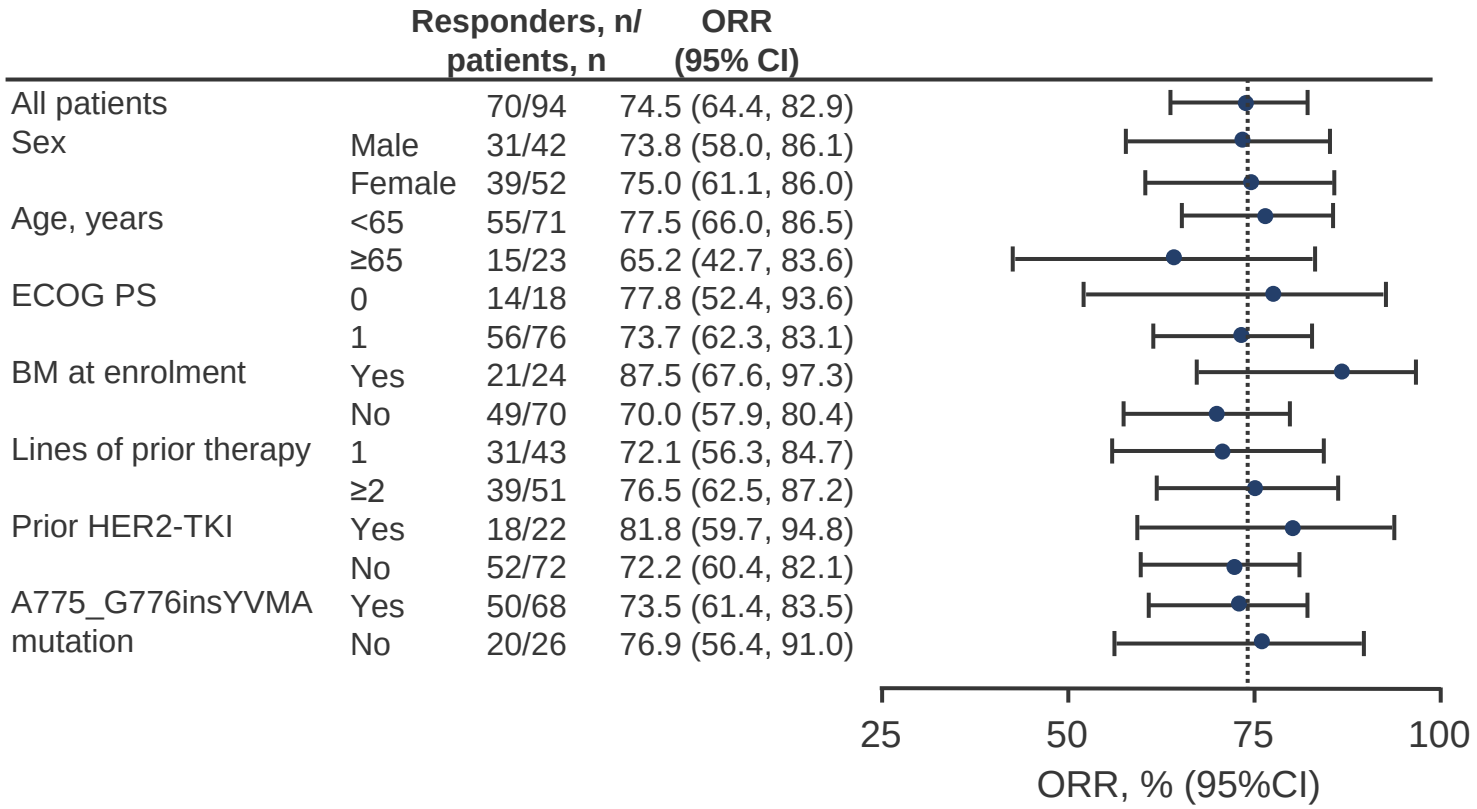
Lu S, et al. AACR; 2025. Abstract nr CT009

CT009: SHR-A1811, a HER2-directed antibody-drug conjugate (ADC), in advanced HER2-mutant non-small cell lung cancer (NSCLC): Updated phase 2 results from HORIZON-Lung – Lu S, et al

- **Key results**

	IRC	Investigator
ORR, % (95%CI)	74.5 (64.4, 82.9)	68.1 (57.7, 77.3)
BOR, n (%)		
PR	70 (74.5)	64 (68.1)
SD	22 (23.4)	27 (28.7)
Non-CR/non-PD	1 (1.1)	0
PD	1 (1.1)	3 (3.2)
DCR, % (95%CI)	98.9 (94.2, 100)	96.8 (91.0, 99.3)
mDoR, mo (95%CI)	9.8 (8.3, 13.9)	9.9 (7.2, 11.5)
TTR, mo (range)	1.4 (1.0–11.2)	1.5 (1.1–10.2)

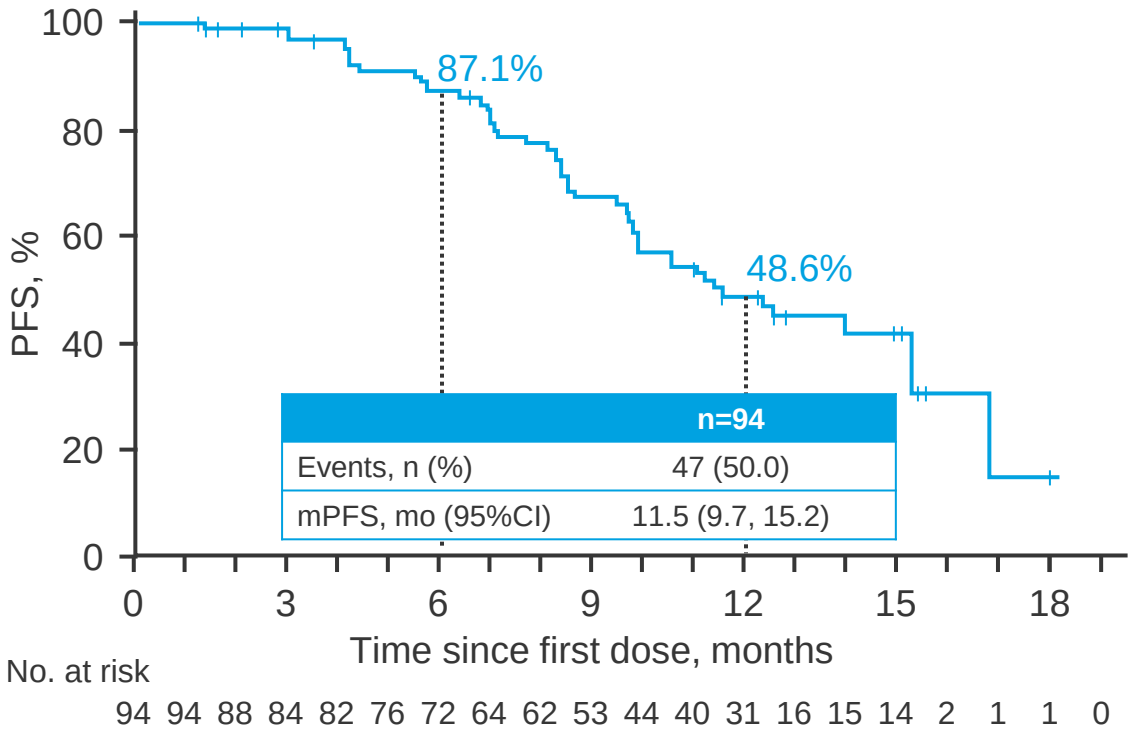
Overall response rate



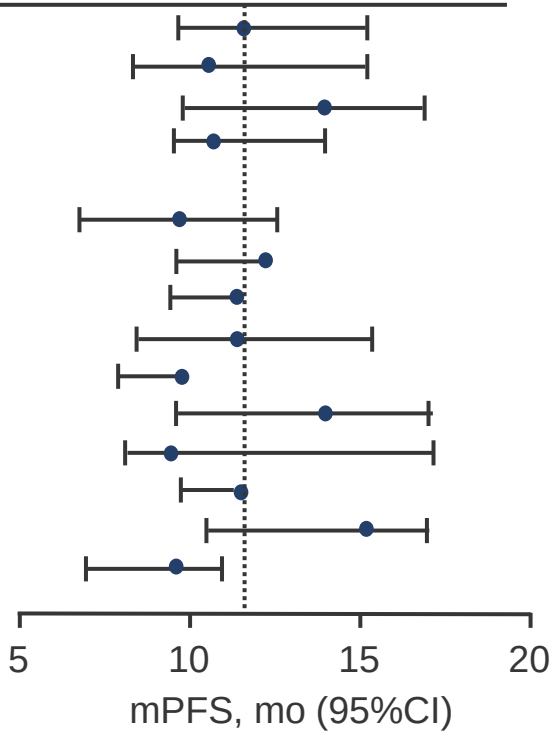
CT009: SHR-A1811, a HER2-directed antibody-drug conjugate (ADC), in advanced HER2-mutant non-small cell lung cancer (NSCLC): Updated phase 2 results from HORIZON-Lung – Lu S, et al

- **Key results (cont.)**

Progression-free survival

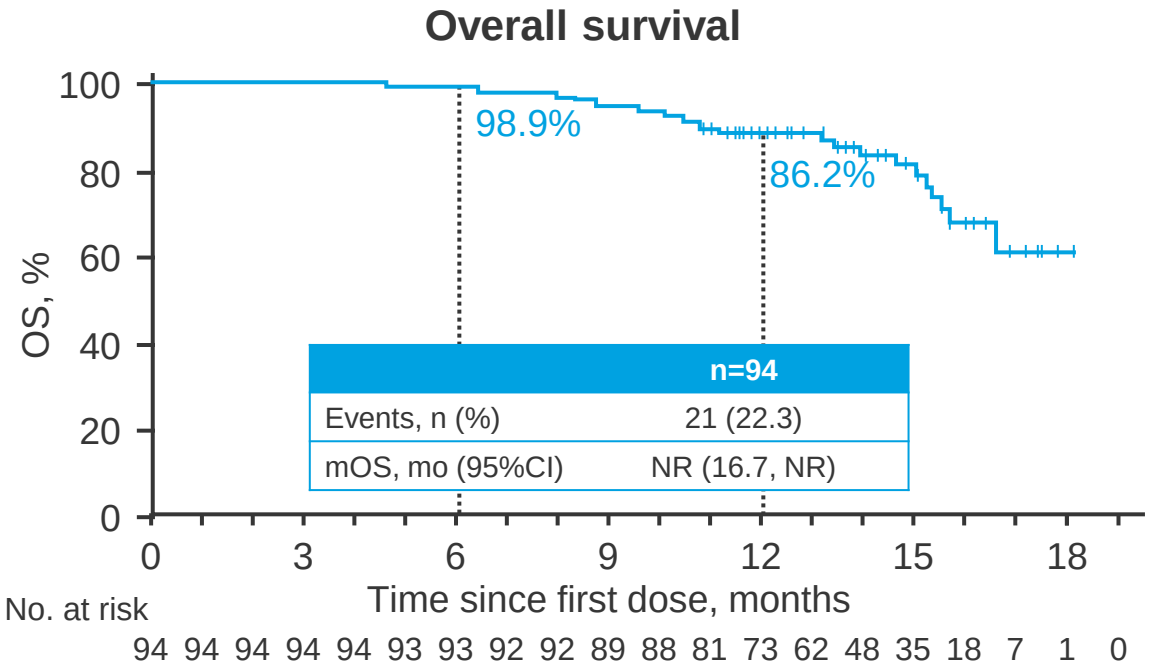


		Events, n/ patients, n	mPFS, mo (95%CI)
All patients		47/94	11.5 (9.7, 15.2)
Sex	Male	25/42	10.6 (8.3, 15.2)
	Female	22/52	13.9 (9.9, 16.8)
Age, years	<65	39/71	10.6 (9.6, 13.9)
	≥65	8/23	NR (8.5, NR)
ECOG PS	0	12/18	9.7 (7.0, 12.5)
	1	35/76	12.3 (9.9, NR)
BM at enrolment	Yes	11/24	11.3 (9.5, NR)
	No	36/70	11.5 (8.5, 15.2)
Lines of prior therapy	1	23/43	9.9 (8.1, NR)
	≥2	24/51	13.9 (9.7, 16.8)
Prior HER2-TKI	Yes	13/22	9.7 (8.3, 16.8)
	No	34/72	11.5 (9.9, NR)
A775_G776insYVMA mutation	Yes	30/68	15.2 (10.6, 16.8)
	No	17/26	9.6 (7.1, 11.1)



CT009: SHR-A1811, a HER2-directed antibody-drug conjugate (ADC), in advanced HER2-mutant non-small cell lung cancer (NSCLC): Updated phase 2 results from HORIZON-Lung – Lu S, et al

- **Key results (cont.)**



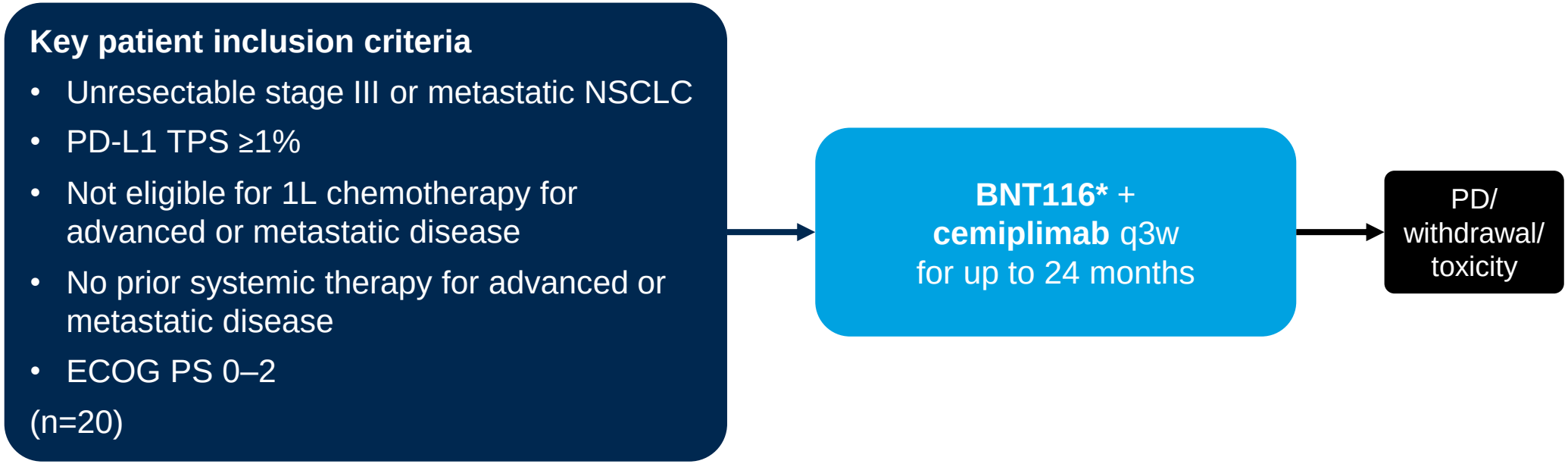
TRAEs, n (%)	n=94
Any	94 (100)
Grade ≥3	63 (67.0)
Led to dose interruption	36 (38.3)
Led to dose reduction	16 (17.0)
Led to discontinuation	2 (2.1)
ILD Grade 1–2 Grade 3	8 (8.5) 7 (7.4) 1 (1.1)

- **Conclusions**
  - In Chinese patients with HER2-mutant NSCLC, trastuzumab rezetecan continued to demonstrate clinical activity across a broad range of patients with a manageable safety profile

Lu S, et al. AACR; 2025. Abstract nr CT009

CT013: Phase I trial evaluating BNT116, a TAA-encoding mRNA vaccine, in combination with cemiplimab in frail patients with advanced non-small cell lung cancer (NSCLC) – Dziadziuszko R, et al

- **Study objective**
  - To evaluate the preliminary antitumor activity and safety of BNT116 (a TAA-encoding mRNA vaccine) + cemiplimab in frail patients with advanced NSCLC in an ongoing phase 1 LuCa-MERIT-1 trial



Primary endpoint

- Safety

Secondary endpoints

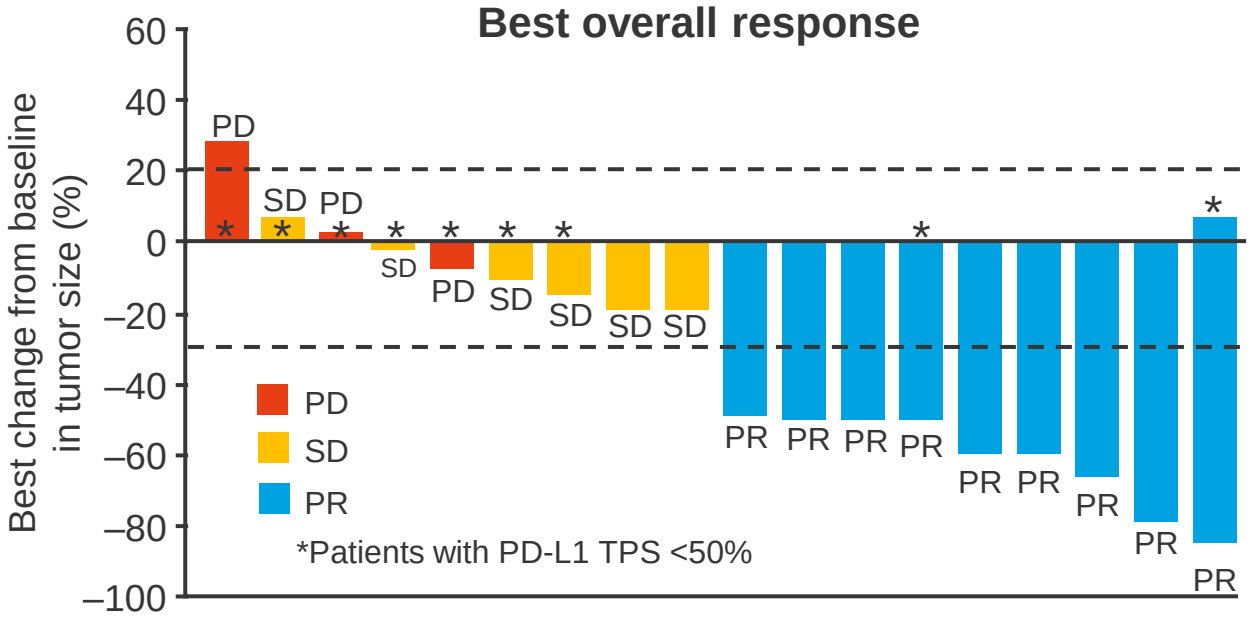
- ORR, PFS, DCR, DoR, DoDC, OS

*Priming 7x q1w then maintenance q3w

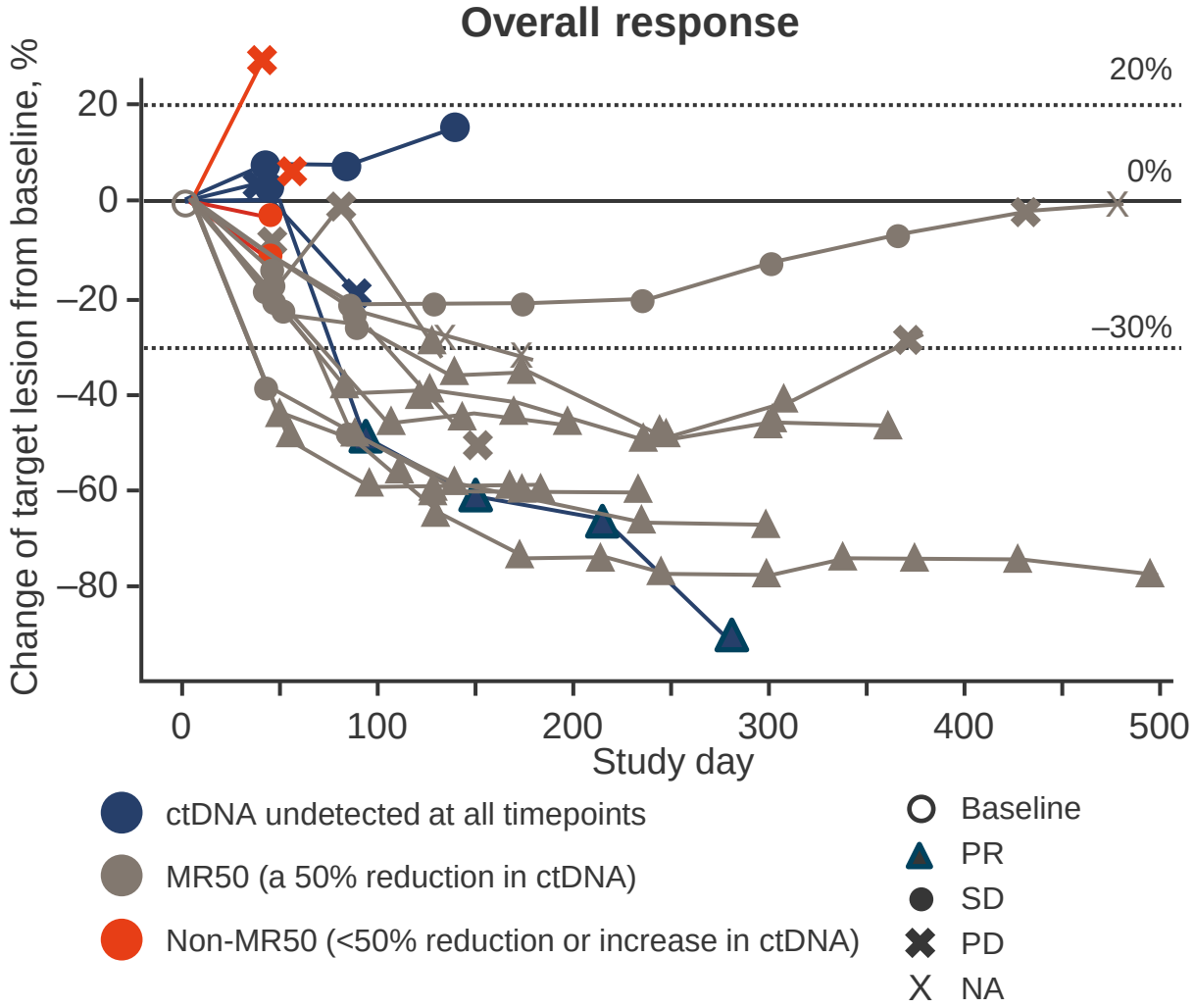
Dziadziuszko R, et al. AACR; 2025. Abstract nr CT013

CT013: Phase I trial evaluating BNT116, a TAA-encoding mRNA vaccine, in combination with cemiplimab in frail patients with advanced non-small cell lung cancer (NSCLC) – Dziadziuszko R, et al

- **Key results**



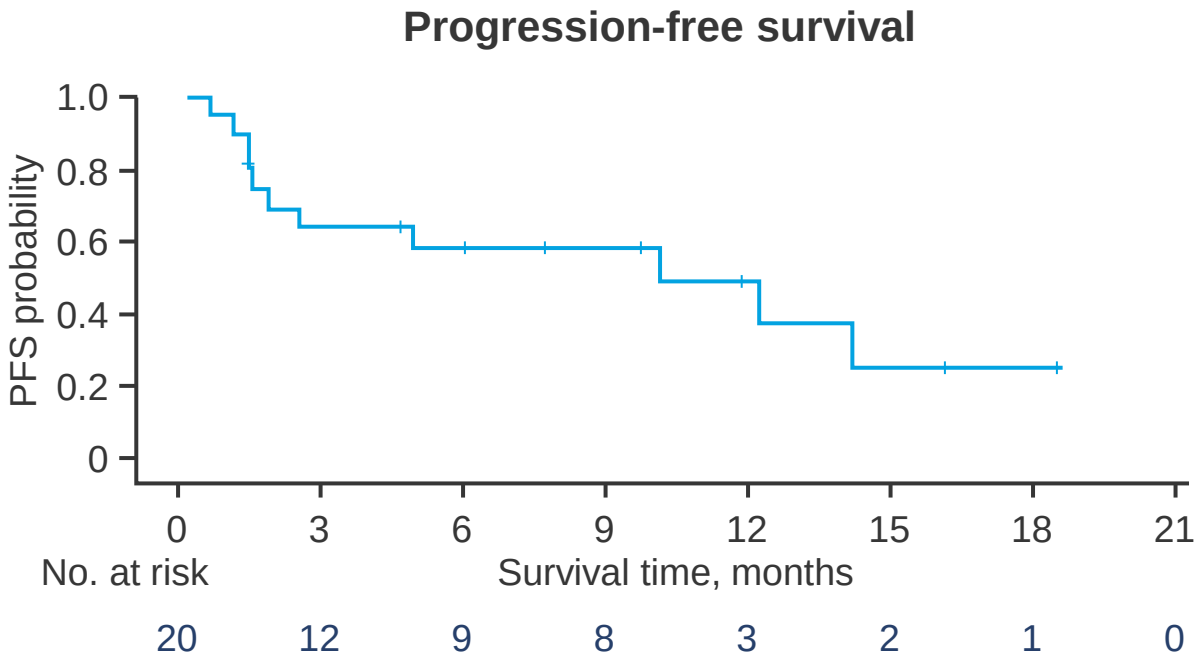
Response, RECIST 1.1, investigator	Frail NSCLC (n=20)
BOR, n (%)	
PR	9 (45)
SD	6 (30)
PD	3 (15)
Missing	2 (10)
ORR, %	45
DCR, %	75

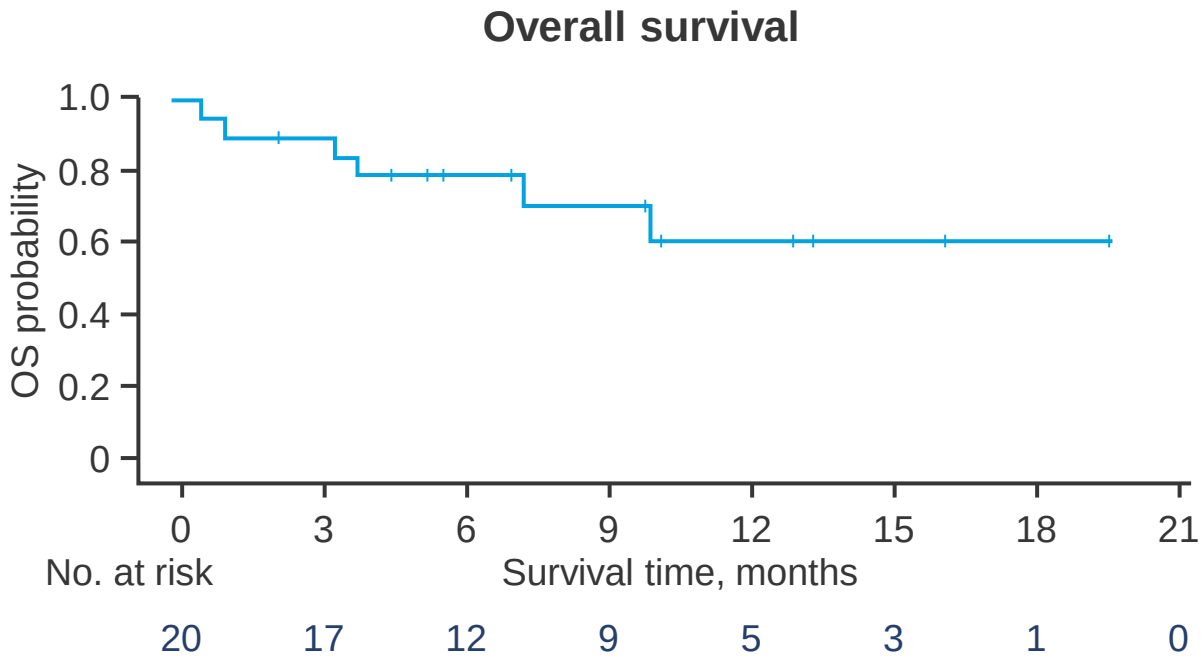


Dziadziuszko R, et al. AACR; 2025. Abstract nr CT013

CT013: Phase I trial evaluating BNT116, a TAA-encoding mRNA vaccine, in combination with cemiplimab in frail patients with advanced non-small cell lung cancer (NSCLC) – Dziadziuszko R, et al

- **Key results (cont.)**





	Frail NSCLC (n=20)
mPFS, mo (95%CI)	9.9 (1.7, NE)
mDoR, mo (95%CI)	NE (6.9, NE)
Median follow-up, mo (range)	7.1 (0.5, 19.3)
mOS, mo (95%CI)	NE (7.2, NE)

Dziadziuszko R, et al. AACR; 2025. Abstract nr CT013

CT013: Phase I trial evaluating BNT116, a TAA-encoding mRNA vaccine, in combination with cemiplimab in frail patients with advanced non-small cell lung cancer (NSCLC) – Dziadziuszko R, et al

- **Key results (cont.)**

TEAEs, n (%)	n=20
Any	20 (100)
Related to BNT116	20 (100)
Related to cemiplimab	13 (65)
Grade ≥3	9 (45)
Related to BNT116	3 (15)
Related to cemiplimab	2 (10)
Serious	8 (40)
Related to BNT116	2 (10)
Related to cemiplimab	3 (15)
Led to death	2 (10)

- **Conclusions**
  - In frail patients with advanced NSCLC, BNT116 + cemiplimab demonstrated preliminary encouraging antitumor activity with an acceptable safety profile