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AACR ANNUAL MEETING

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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 2022. This slide set specifically focuses on the **AACR Annual Meeting 2022** and is available in 4 languages – English, French, Chinese and Japanese.

The area of clinical research in oncology is a challenging and ever 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 Solange Peters and Enriqueta Felip 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 2022

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 strategies
  - Targeted therapies
- Other malignancies
  - SCLC, mesothelioma and thymic epithelial tumors

Screening, biomarkers and prevention

645: Heterogeneity of immunotherapy biomarkers in the TRACERx non-small cell lung cancer multi-region lung cancer cohort study – Hiley CT, et al

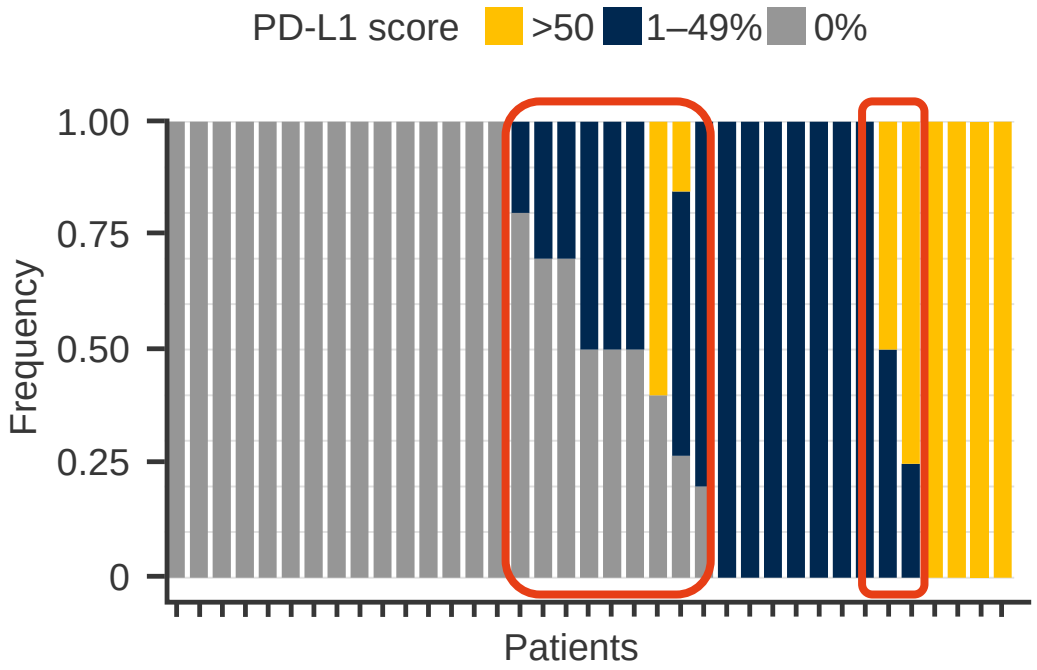
- **Study objective**
  - To evaluate the impact of intratumor heterogeneity on established and putative immunotherapy biomarkers in patients with NSCLC from the TRACERx study

- **Methods**
  - Whole exome sequencing was performed on 432 primary tumors from 421 patients providing 1553 unique tumor regions and RNA sequencing on 269 samples providing 782 regions
    - Single genes: CD274, CD38, CD8A, CXCL13, CXCL9, HAVCR2, IGLL5, IGALS9, MEX3B, MZB1
    - Gene expression signature (2 groups): IPRES, IMPRES, TIDE, cytolytic score, T effector score, T effector score (POPLAR), TGF-β response signature, EMT, COX-UIS, T-cell inflamed, HLA class 1 & 2, chemokine
    - Gene expression signature (3 groups): proliferation, tertiary lymphoid structures (TLS)
  - TMB was determined with high TMB defined as ≥10 mut/Mb
  - PD-L1 IHC was assessed on whole slide (22c3) and by spatially separated multi-region (CD274) expression

645: Heterogeneity of immunotherapy biomarkers in the TRACERx non-small cell lung cancer multi-region lung cancer cohort study – Hiley CT, et al

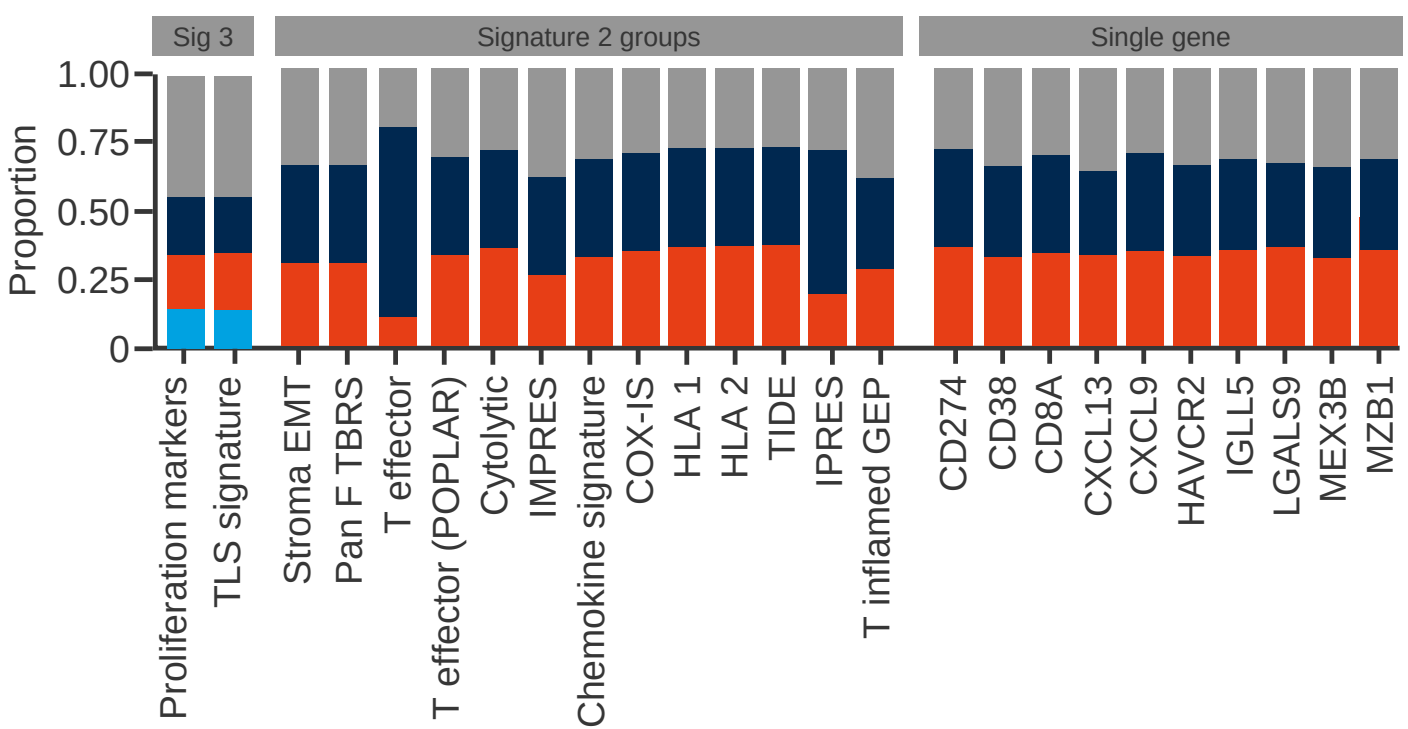
- **Key results**

Tissue microarray of 108 spatially separated primary tumor regions (n=36)



- 28% of tumors had discordant PD-L1 IHC

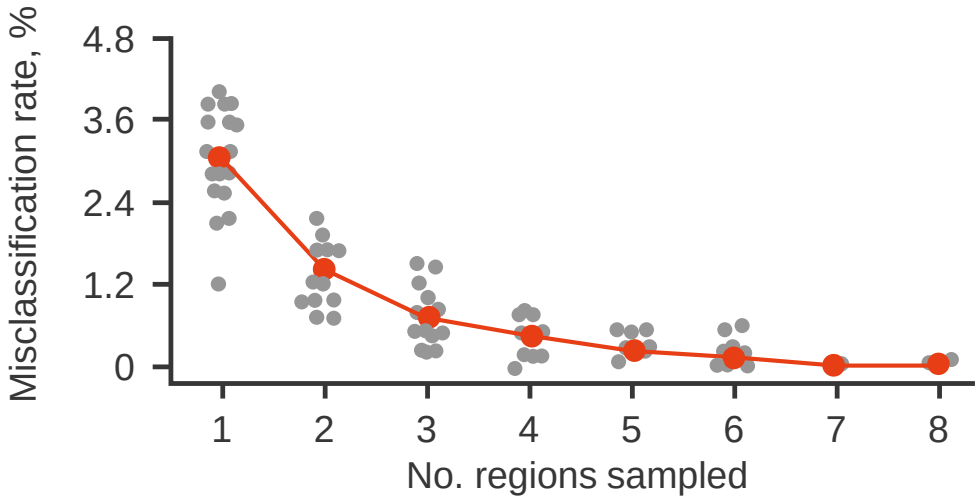
Gene expression biomarker discordance



- 20–45% discordance rate in primary regions

645: Heterogeneity of immunotherapy biomarkers in the TRACERx non-small cell lung cancer multi-region lung cancer cohort study – Hiley CT, et al

- **Key results (cont.)**
  - 20% of patients with high TMB tumors had ≥1 region below TMB threshold (10 mut/Mb)
  - 3% of patients tumors were misclassified which was associated with higher stage and history of smoking



- **Conclusions**
  - In patients with NSCLC, there is significant heterogeneity of immune biomarkers and this may explain the responses observed in biomarker negative populations in clinical trials
  - Biomarkers are required that are not impacted by intratumor heterogeneity such as clonal TMB or more comprehensive tumor sampling

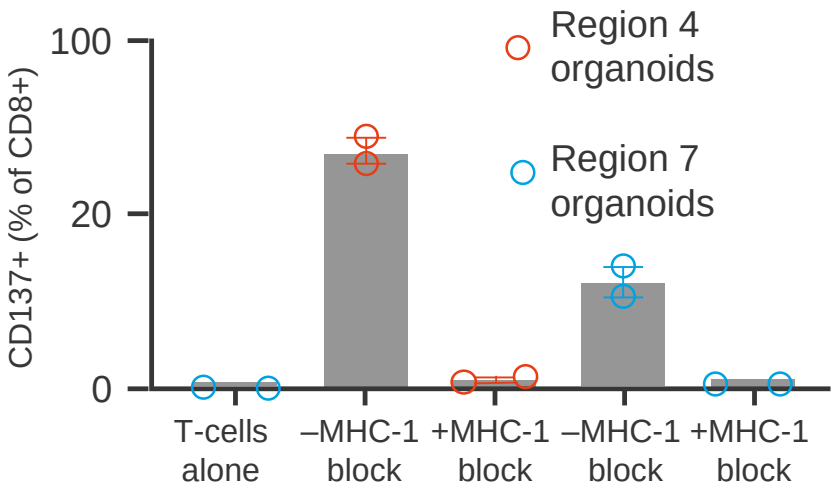
692: Patient-derived co-cultures of TRACERx lung cancer organoids and autologous T-cells reveal heterogeneity in immune evasion between cancer subclones – Dijkstra KK, et al

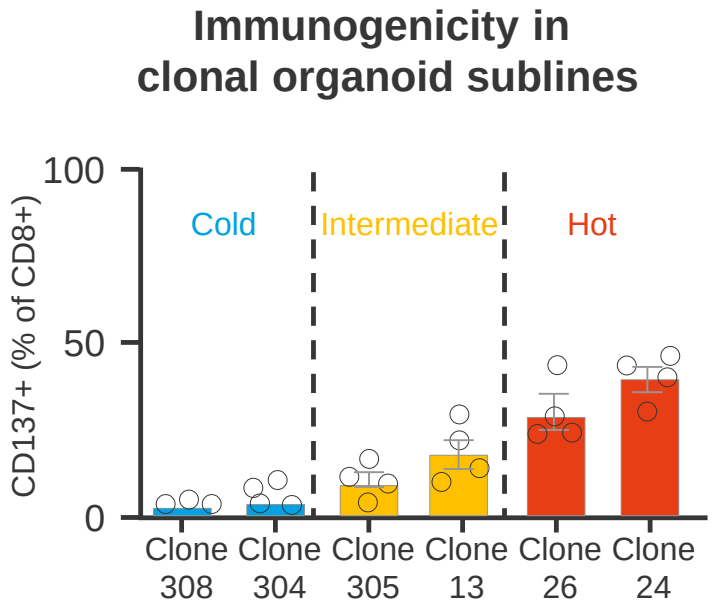
- **Study objective**
  - To evaluate intratumor heterogeneity in individual patients with NSCLC from the TRACERx study using a co-culture system of cancer organoids and autologous T-cells

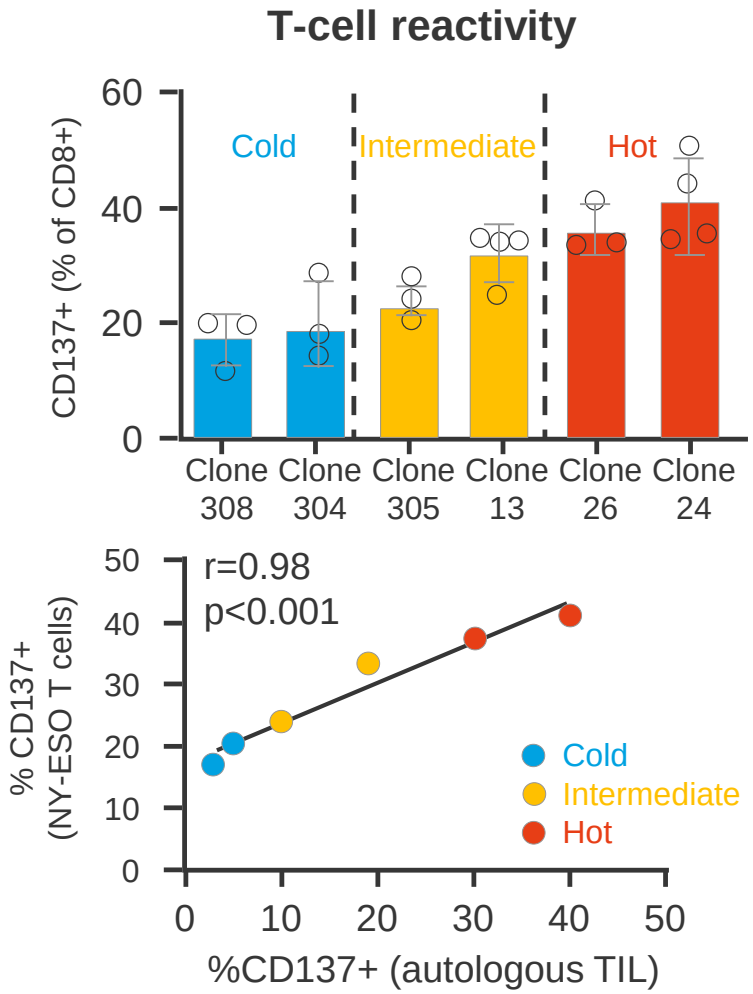
- **Methods**
  - A patient-derived study platform was generated using >20 separate NSCLC organoid lines based on the isolation of individual clonal organoids from multiple spatially separated tumor regions to evaluate T-cell responses in the individual cancer subclones
  - T-cell responses were assessed by co-culturing each organoid subline with autologous TILs

692: Patient-derived co-cultures of TRACERx lung cancer organoids and autologous T-cells reveal heterogeneity in immune evasion between cancer subclones – Dijkstra KK, et al

- **Key results**



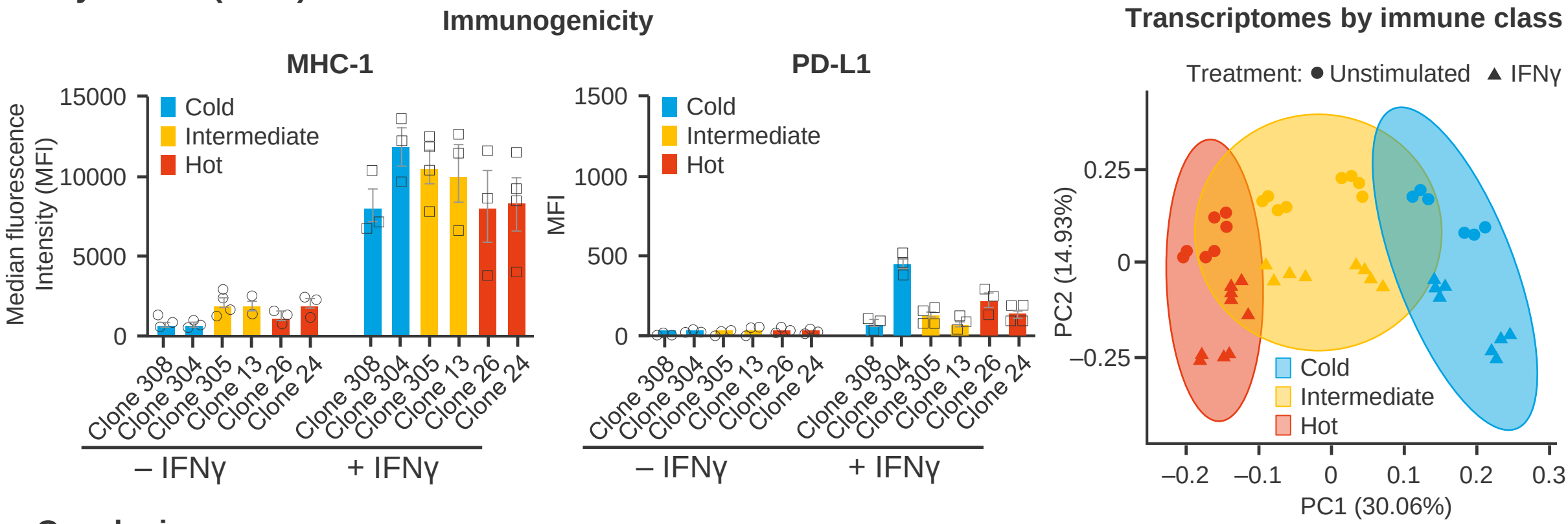




- Data are from a 77-year-old male patient who had stage IIb poorly differentiated adenosquamous carcinoma
- Tissue extracted from his primary tumor provided 14 clones biobanked in Region 4 and 8 clones biobanked in Region 7
- Frozen TILs from region 7 were cultured for 21 days and stimulated weekly with organoids (Region 4 and 7 mix) to produce a rapid expansion of T cells
- TIL activation was measured using 4-1BB (CD137 expression)
- Immune evading subclones were identified and multi-omics used to characterize immune sensitive and resistant sublines

692: Patient-derived co-cultures of TRACERx lung cancer organoids and autologous T-cells reveal heterogeneity in immune evasion between cancer subclones – Dijkstra KK, et al

- **Key results (cont.)**



- **Conclusions**
  - Multiple clonal organoid sublines from individual patients with NSCLC can be established and showed heterogeneity between and within tumor regions in terms of eliciting T cell activation

727: Detection of early-stage lung cancer using a liquid biopsy test based on extracellular vesicle proteins – Hinestrosa JP, et al

- **Study objective**
  - To evaluate whether a liquid biopsy test using extracellular vesicle (EV) proteins can be used to detect early stage NSCLC

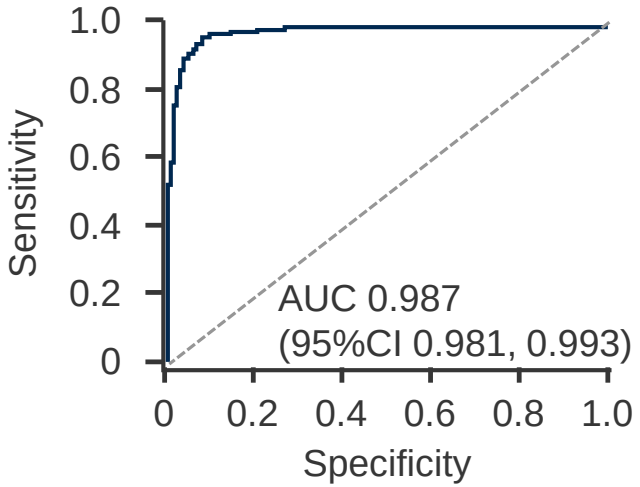
- **Methods**
  - Proteins associated with EV were isolated using an alternating current electokinetic system from the blood of patients with stage I–IV NSCLC (n=161) and controls (n=683)
  - A multiplex ELISA was used to assess EV protein concentration and quantify EV protein biomarker information for each individual
  - To identify the most important features for differentiation of NSCLC and control samples, a machine learning algorithm was developed based on recursive feature elimination with cross-validation for sensitivity and specificity

727: Detection of early-stage lung cancer using a liquid biopsy test based on extracellular vesicle proteins – Hinestrosa JP, et al

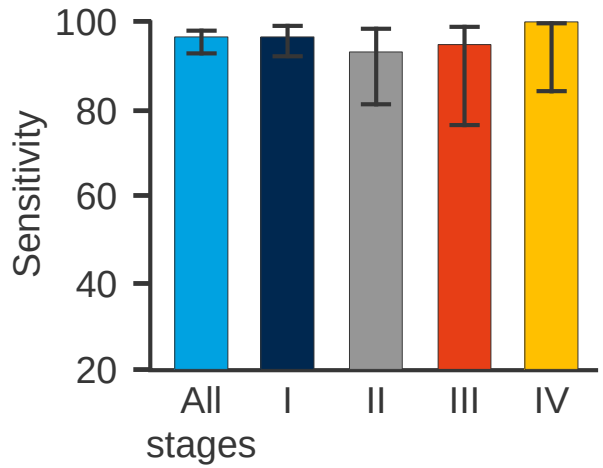
- **Key results (cont.)**

	Lung cancer (n=161)	Controls (n=683)
Female, %	42	52
Median age, years	63	58
Smokers, %	41	12
Stage, n		
I	88	-
II	34	-
III	20	-
IV	19	-

EV assay performance



Multi-marker algorithm for optimal performance. Threshold for 92% specificity selected



Error bars represent the two-sided 95% Wilson confidence interval

- 97% sensitivity
- 92% specificity

- **Conclusions**
  - Extracellular vesicle protein biomarkers are capable of detecting early stage lung cancer and this liquid biopsy assay may be suitable in the diagnosis of NSCLC

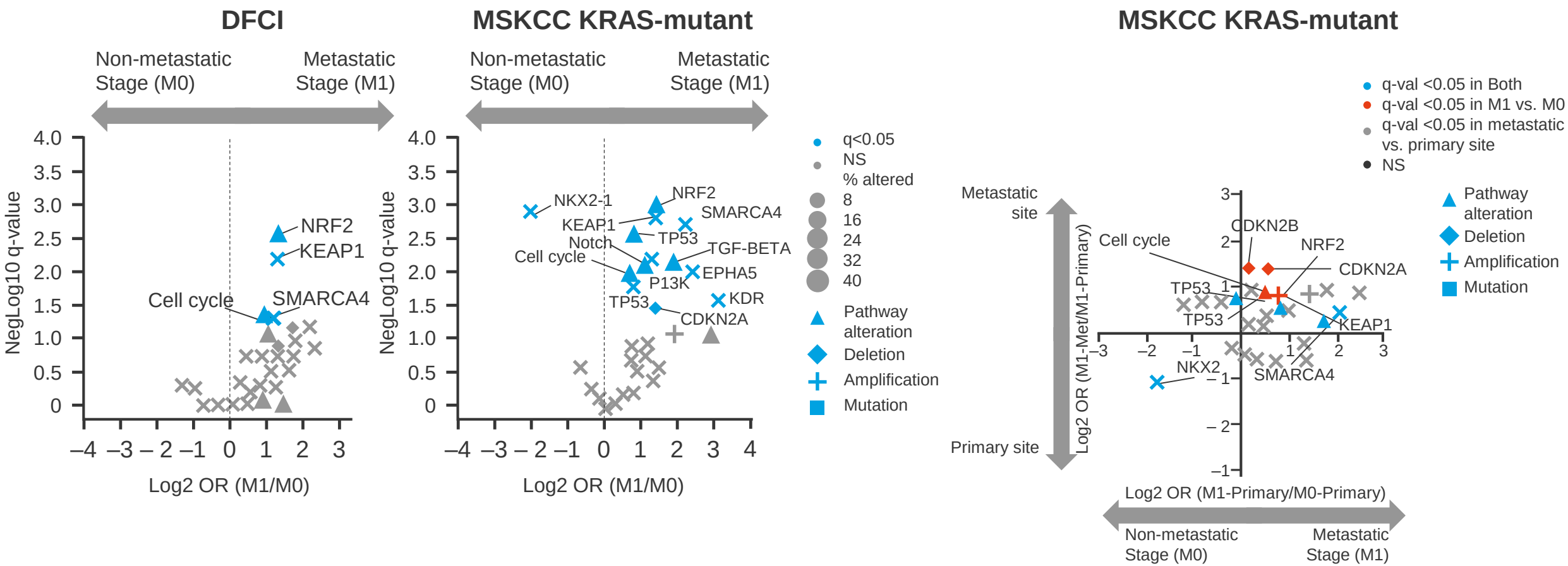
2181: Genomic correlates of metastasis in KRAS mutant lung adenocarcinoma – Boiarsky D, et al

- **Study objective**
  - To evaluate clinical and genomic predictors of metastasis in patients with KRAS-mutant lung adenocarcinoma

- **Methods**
  - Samples were collected from patients with KRAS-mutant lung adenocarcinoma who were profiled with NGS (OncoPanel; n=616) at the Dana-Farber Cancer Institute (DFCI) and the findings validated using samples profiled using MSK-IMPACT in the AACR GENIE database (KRAS-mutant, n=1342 and KRAS WT, n=2722) at the Memorial Sloan Kettering Cancer Center (MSKCC)
  - A transcriptional exploration was undertaken on TCGA (KRAS-mutant, n=152 and KRAS WT, n=348)
  - Stage, histology, RFS and OS were assessed

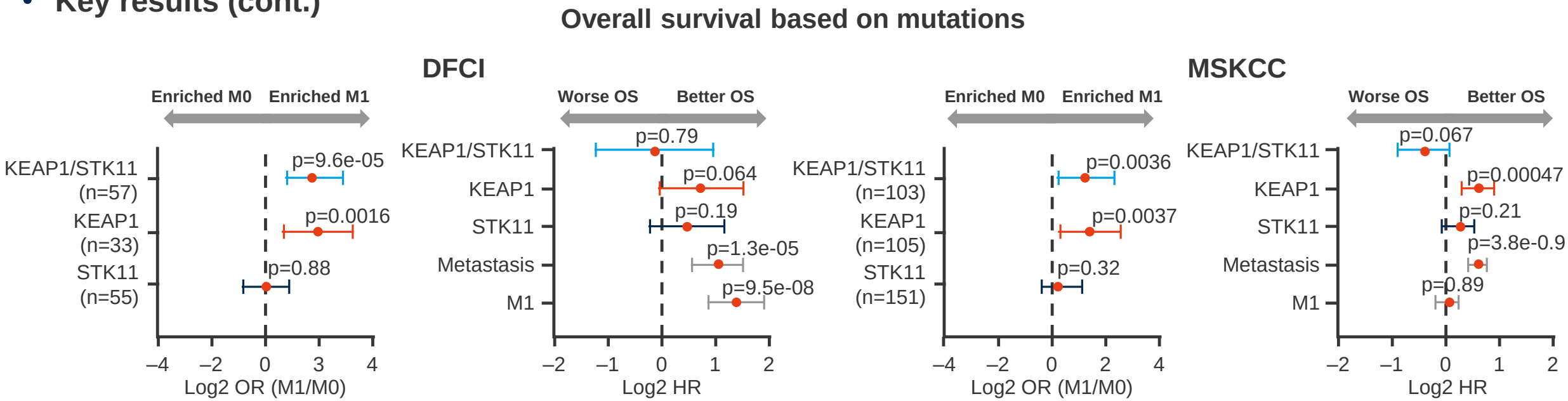
2181: Genomic correlates of metastasis in KRAS mutant lung adenocarcinoma – Boiarsky D, et al

- **Key results**



2181: Genomic correlates of metastasis in KRAS mutant lung adenocarcinoma – Boiarsky D, et al

- **Key results (cont.)**



- **Conclusions**
  - In patients with lung adenocarcinoma, KEAP1 and STK11 mutations are associated with poorer OS, while KEAP1 mutations and KEAP1/STK11 co-mutations, but not STK11, mutations are associated with metastasis

3580: Integrative genomics of checkpoint blockade response in advanced non-small cell lung cancer – Ravi A, et al

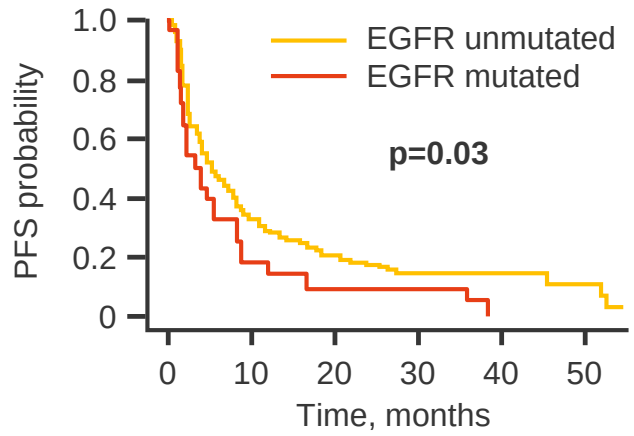
- **Study objective**
  - To evaluate the molecular features associated with responses to PD-(L)1 inhibitors in patients with advanced NSCLC in the Stand Up 2 Cancer-Mark Foundation (SU2C-MARK) cohort

- **Methods**
  - Pre-treatment biopsies from 393 patients with NSCLC were collected for whole exome (n=309) and/or RNA sequencing (n=153) and responses to PD-(L)1 inhibitors assessed in comparison to matched normal tissue to examine genomic alterations, immune microenvironment and tumor intrinsic expression

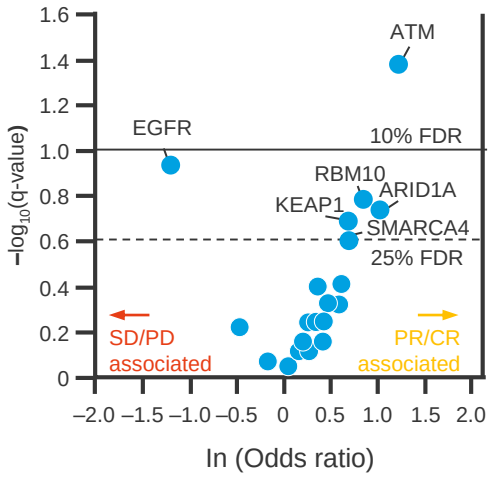
3580: Integrative genomics of checkpoint blockade response in advanced non-small cell lung cancer – Ravi A, et al

- **Key results**

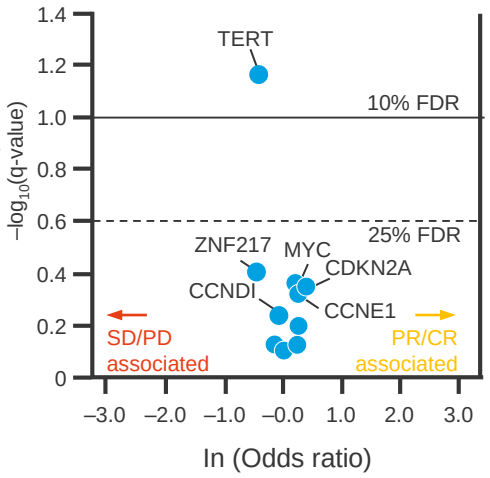
PFS by EGFR status



Somatic mutations

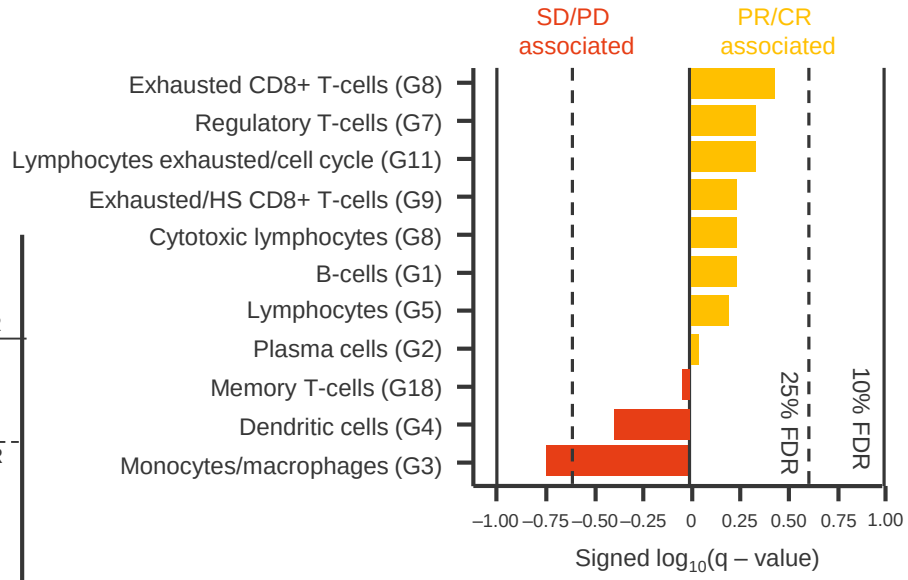


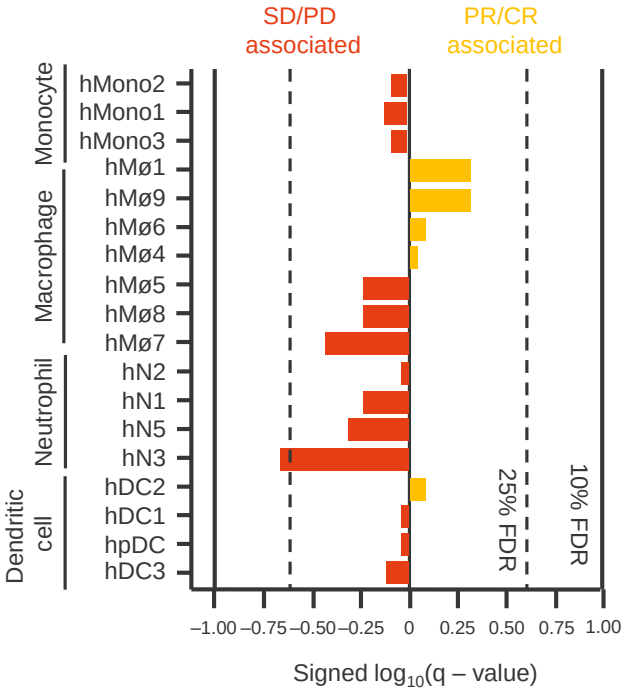
Gene level CN



Expression analysis

SD/PD associated genes	PR/CR associated genes
PDLIM3, CTB-56J15.1, NR4A1, LGR5, BCHE, TBX5	PSME2P2, RP11-27E7.2, VGF, CD274, PSMB9, CXCL9, TRBV9, CXCL11, AZGP1

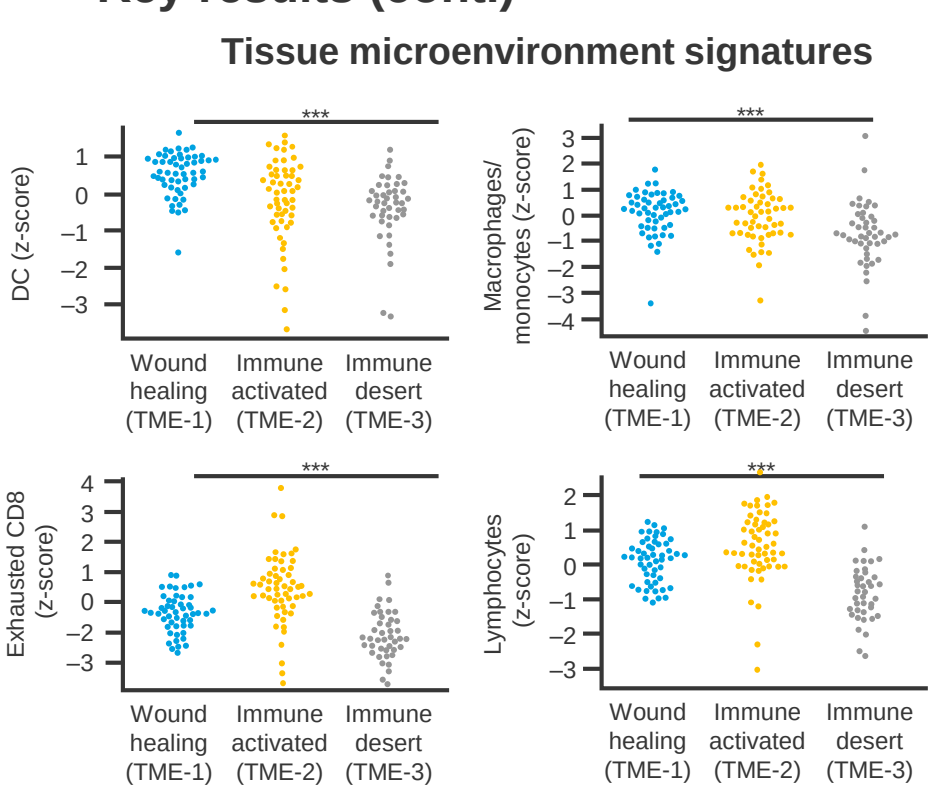


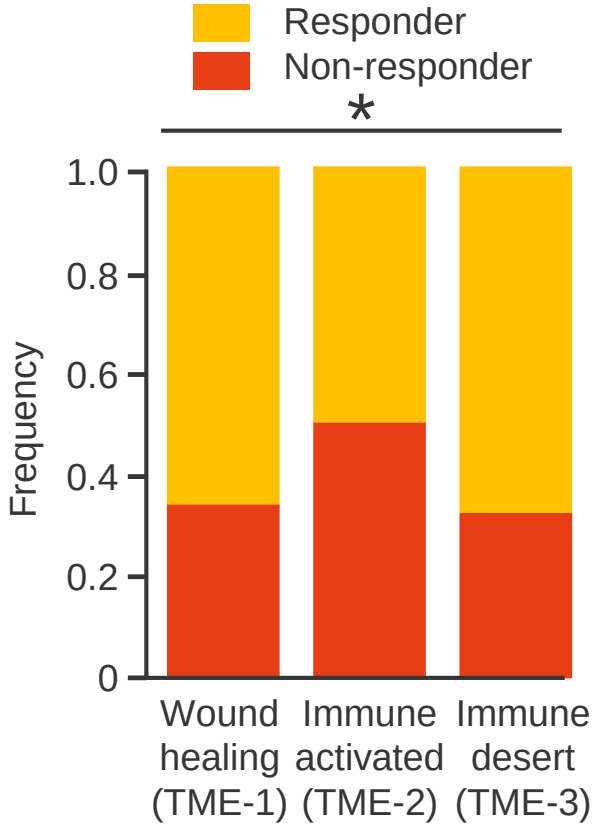


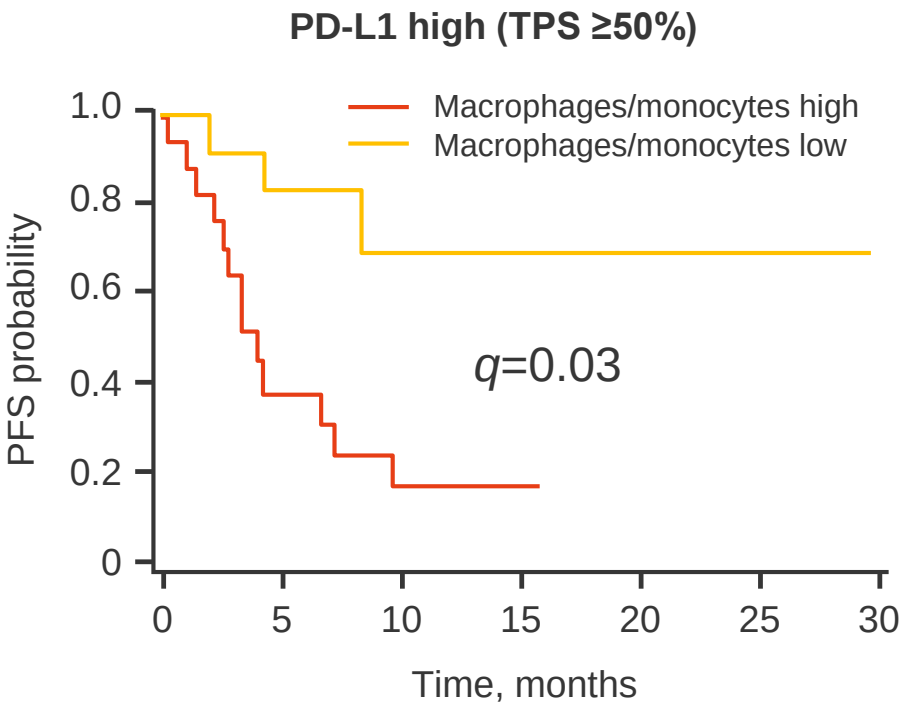
Ravi A, et al. AACR; 2022. Abstract nr 3580

3580: Integrative genomics of checkpoint blockade response in advanced non-small cell lung cancer – Ravi A, et al

- **Key results (cont.)**







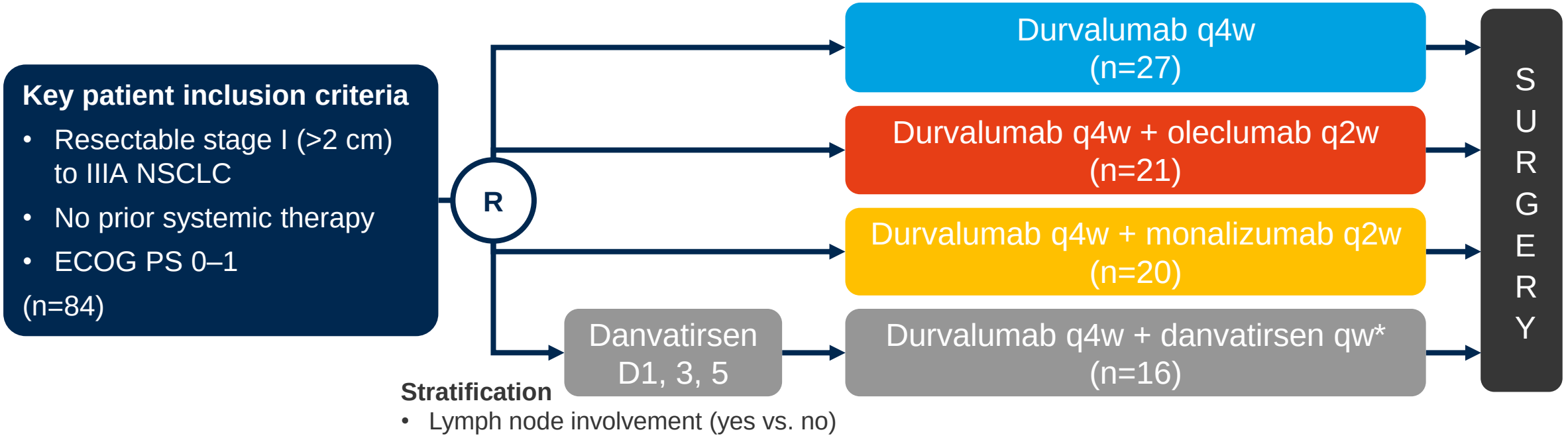
- **Conclusions**
  - In patients with NSCLC, EGFR mutations and TERT amplification were found to be the top genomic alterations associated with resistance, while wound healing and immune desert transcriptional states were present prior to checkpoint blockade and also associated with resistance

Ravi A, et al. AACR; 2022. Abstract nr 3580

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

CT011: NeoCOAST: open-label, randomized, phase 2, multidrug platform study of neoadjuvant durvalumab alone or combined with novel agents in patients (pts) with resectable, early-stage non-small-cell lung cancer (NSCLC) – Cascone T, et al

- **Study objective**
  - To evaluate the efficacy and safety of one 28-day cycle of neoadjuvant durvalumab alone or combined with oleclumab (an anti-CD73), monalizumab (an anti-NKG2A) or danvatirsen (an anti-STAT3 antisense oligonucleotide) in patients with resectable, early stage NSCLC in the NeoCOAST study



Primary endpoint

- MPR rate

Secondary endpoints

- pCR rate, safety

*Arm closed early as development program discontinued

Cascone T, et al. AACR; 2022. Abstract nr CT011

CT011: NeoCOAST: open-label, randomized, phase 2, multidrug platform study of neoadjuvant durvalumab alone or combined with novel agents in patients (pts) with resectable, early-stage non-small-cell lung cancer (NSCLC) – Cascone T, et al

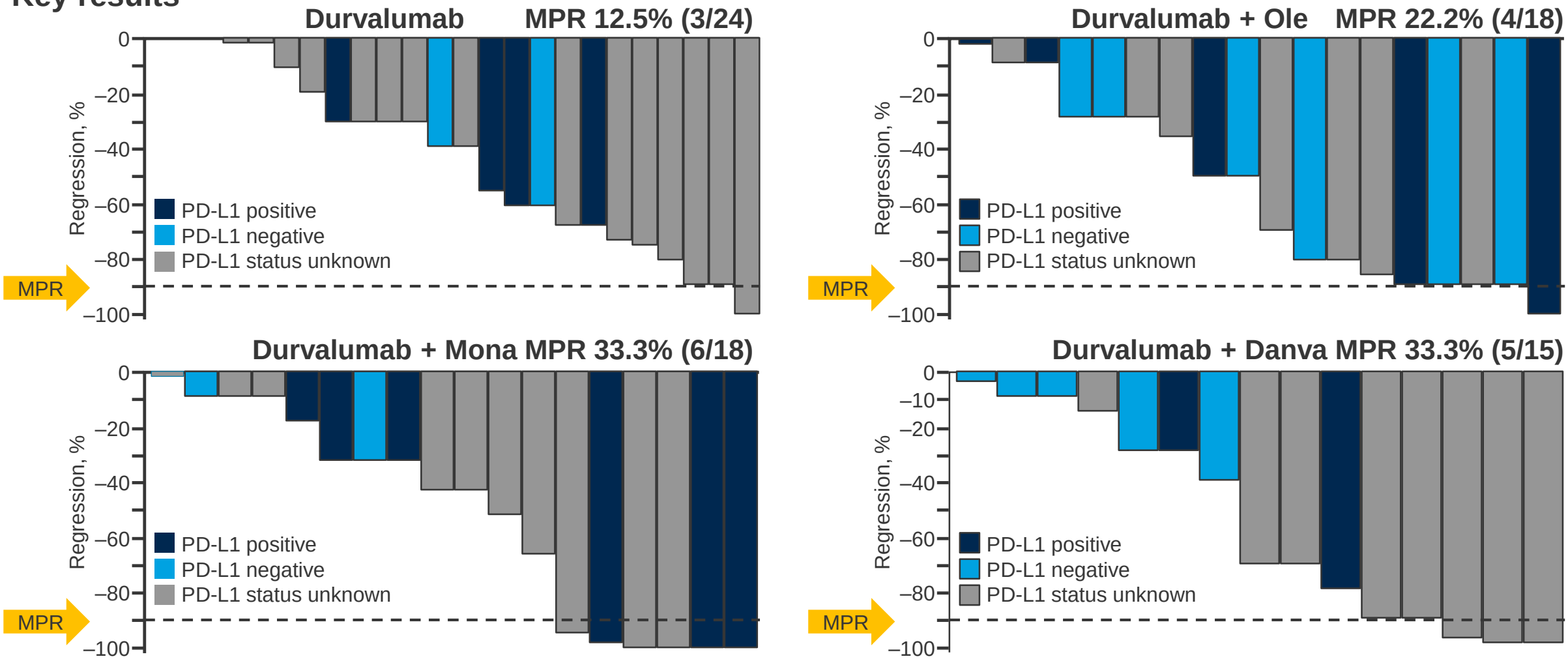
- **Key results**

Responses, n (%)	Durvalumab (n=27)	Durvalumab + oleclumab (n=21)	Durvalumab + monalizumab (n=20)	Durvalumab + danvatirsen (n=16)
MPR	3 (11.1)	4 (19.0)	6 (30.0)	5 (31.3)
pCR	1 (3.7)	2 (9.5)	2 (10.0)	2 (12.5)
ORR	2 (7.4)	1 (4.8)	3 (15.0)	1 (6.3)
BOR				
PR	2 (7.4)	1 (4.8)	3 (15.0)	1 (6.3)
SD	22 (81.5)	17 (81.0)	15 (75.0)	14 (87.5)
PD	1 (3.7)	3 (14.3)	1 (5.0)	1 (6.3)
NE	1 (3.7)	0	1 (5.0)	0

Cascone T, et al. AACR; 2022. Abstract nr CT011

CT011: NeoCOAST: open-label, randomized, phase 2, multidrug platform study of neoadjuvant durvalumab alone or combined with novel agents in patients (pts) with resectable, early-stage non-small-cell lung cancer (NSCLC) – Cascone T, et al

- **Key results**



Patients without biopsy specimens at surgery are excluded. PD-L1 positive defined as tumor cell ≥1% and PD-L1 negative as tumor cell <1%

CT011: NeoCOAST: open-label, randomized, phase 2, multidrug platform study of neoadjuvant durvalumab alone or combined with novel agents in patients (pts) with resectable, early-stage non-small-cell lung cancer (NSCLC) – Cascone T, et al

- **Key results (cont.)**
  - Surgery was completed without significant delay in 76/83 (91.6%) patients, while 7 patients were unable to complete surgery (PD/stage IV disease, n=5; lost to follow-up, n=1 and SAE of pneumonia, n=1)

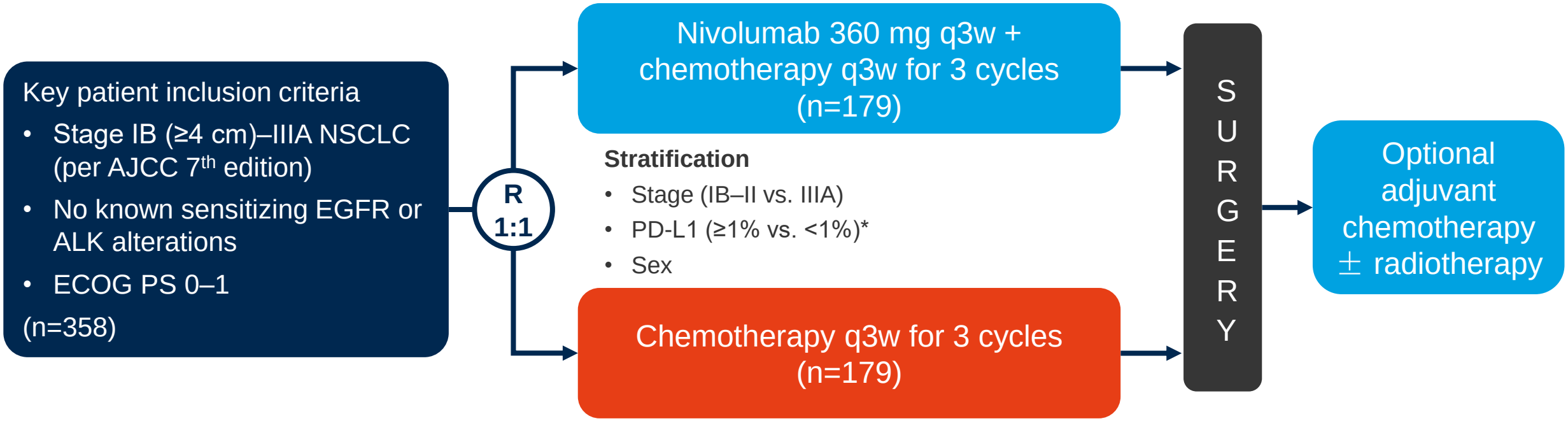
AEs, n (%)	Durvalumab (n=26)	Durvalumab + oleclumab (n=21)	Durvalumab + monalizumab (n=20)	Durvalumab + danvatirsen (n=16)
Any TEAE	18 (69.2)	19 (90.5)	15 (75.0)	13 (81.3)
Grade ≥3	5 (19.2)	3 (14.3)	2 (10.0)	5 (31.3)
Any TRAE	9 (34.6)	12 (57.1)	10 (50.0)	7 (43.8)
Grade ≥3	0	1 (4.8)	0	1 (6.3)
Serious	1 (3.8)	1 (4.8)	0	1 (6.3)
Led to discontinuation	0	1 (4.8)	1 (5.0)	1 (6.3)
Led to death	0	0	0	1 (6.3)

- **Conclusions**
  - In patients with resectable, early stage NSCLC, neoadjuvant durvalumab combined with oleclumab, monalizumab or danvatirsen demonstrated numerical improvements in MPR compared with durvalumab alone and the safety profile was similar in all treatment arms

Cascone T, et al. AACR; 2022. Abstract nr CT011

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Study objective**
  - To evaluate the EFS and OS with neoadjuvant nivolumab + platinum-based chemotherapy in patients with resectable NSCLC at an interim analysis of the CheckMate 816 study



Primary endpoints

- pCR (0% viable tumor cells in lung and lymph nodes), EFS

Secondary endpoints

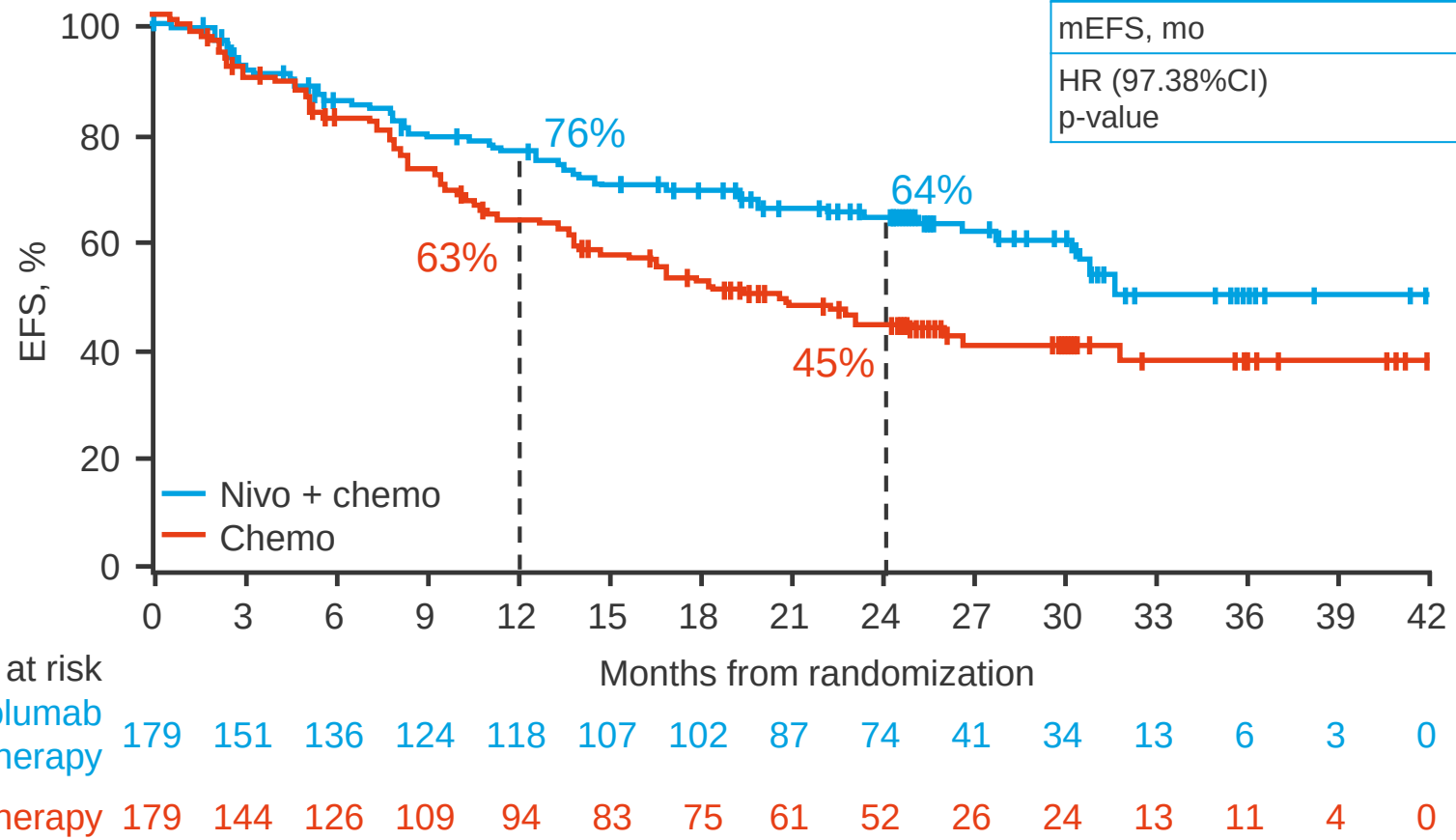
- MPR, OS, safety

*Determined by the PD-L1 28-8 pharmDx assay

Girard N, et al. AACR; 2022. Abstract nr CT012

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Key results**



	Nivo + chemo (n=179)	Chemo (n=179)
mEFS, mo	31.6	20.8
HR (97.38%CI)	0.63 (0.43, 0.91)	
p-value	0.0052	

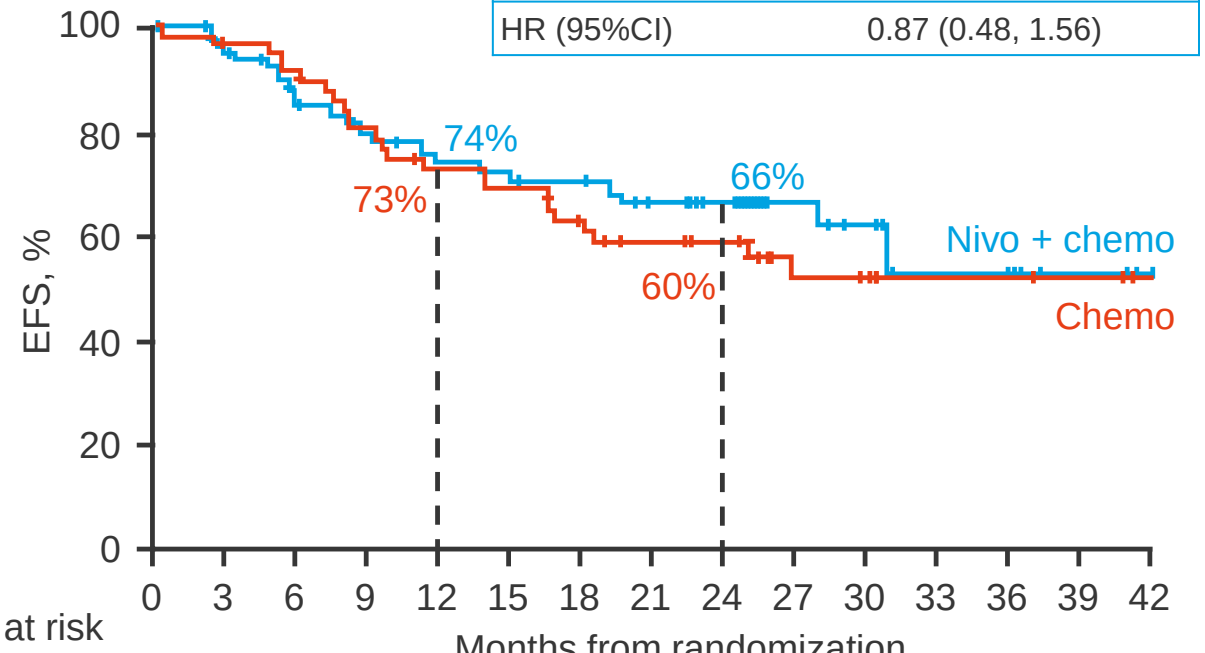
Girard N, et al. AACR; 2022. Abstract nr CT012

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Key results (cont.)**

Stage IB–II

	Nivo + chemo (n=65)	Chemo (n=62)
mEFS, mo	NR	NR
HR (95%CI)	0.87 (0.48, 1.56)	

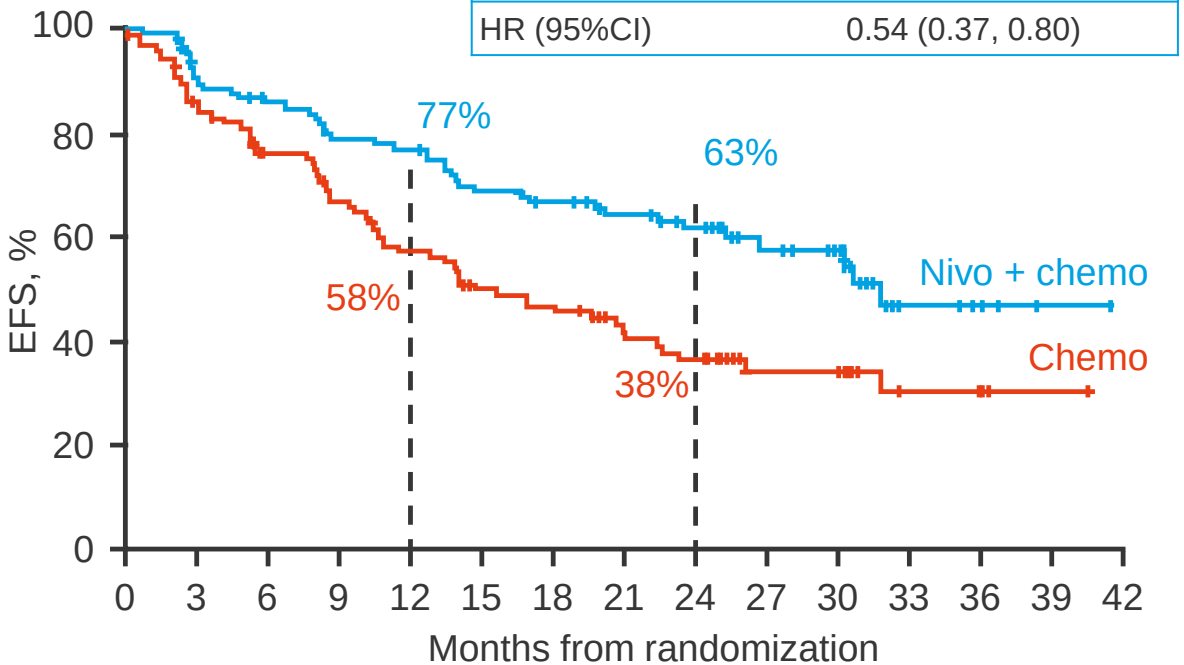


No. at risk

Nivo + chemo	65	56	47	43	39	37	36	31	27	15	12	4	2	1	0
Chemo	62	55	51	44	39	37	32	28	23	12	10	8	6	3	0

Stage IIIA

	Nivo + chemo (n=113)	Chemo (n=115)
mEFS, mo	31.6	15.7
HR (95%CI)	0.54 (0.37, 0.80)	



Nivo + chemo	113	95	89	81	79	70	66	56	47	26	22	9	4	2	0
Chemo	115	89	75	65	55	46	43	33	29	14	14	5	5	1	0

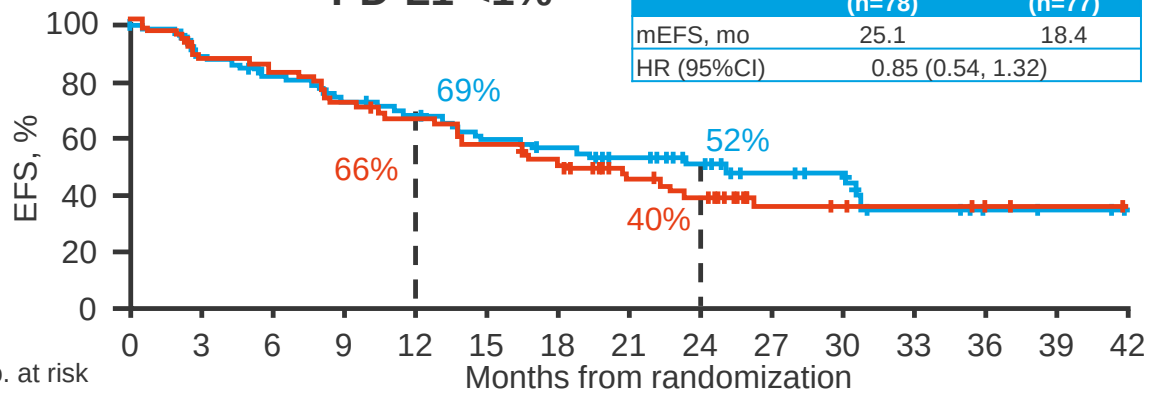
Girard N, et al. AACR; 2022. Abstract nr CT012

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Key results (cont.)**

PD-L1 <1%

	Nivo + chemo (n=78)	Chemo (n=77)
mEFS, mo	25.1	18.4
HR (95%CI)	0.85 (0.54, 1.32)	

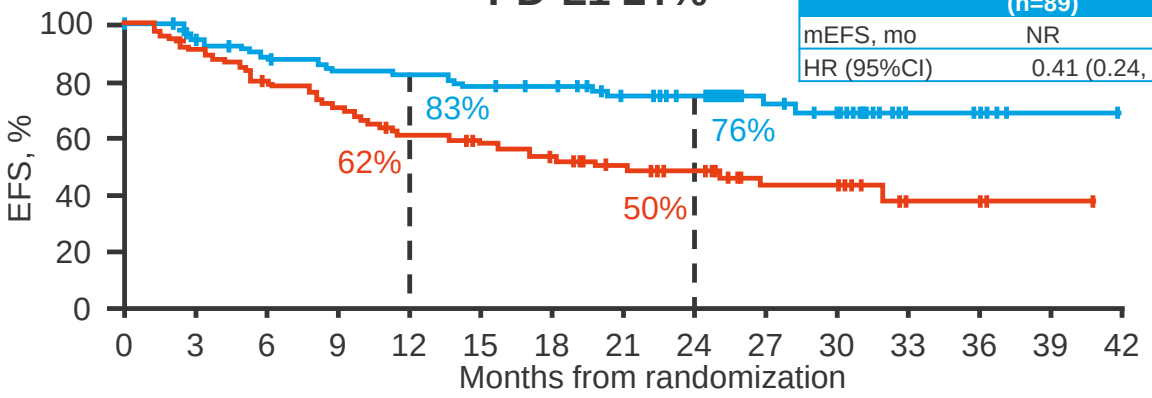


No. at risk

Nivo + chemo	78	65	57	51	46	39	36	30	24	15	13	6	3	2	0
Chemo	77	62	58	49	44	38	34	25	21	10	9	8	6	3	0

PD-L1 ≥1%

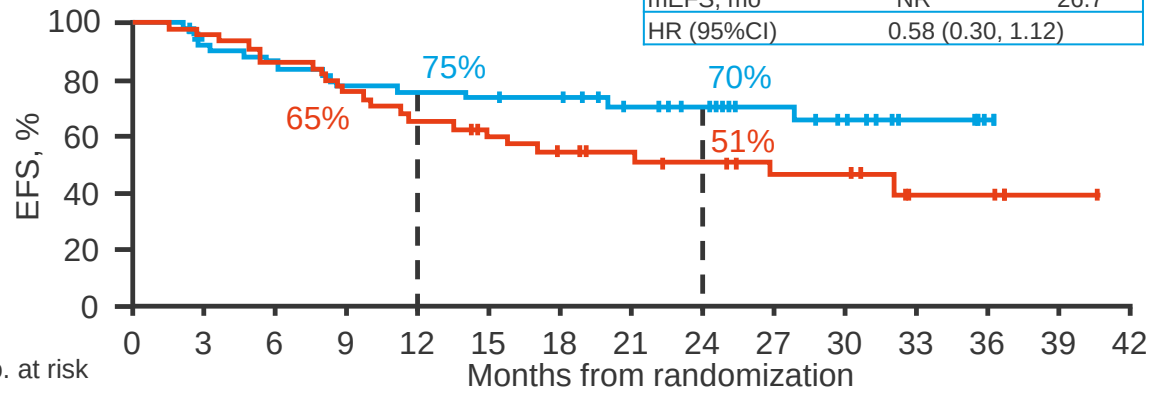
	Nivo + chemo (n=89)	Chemo (n=89)
mEFS, mo	NR	21.1
HR (95%CI)	0.41 (0.24, 0.70)	



Nivo + chemo	89	76	69	66	65	62	60	53	47	24	19	7	3	1	0
Chemo	89	71	60	53	45	41	37	32	27	16	15	5	5	1	0

PD-L1 1–49%

	Nivo + chemo (n=51)	Chemo (n=47)
mEFS, mo	NR	26.7
HR (95%CI)	0.58 (0.30, 1.12)	

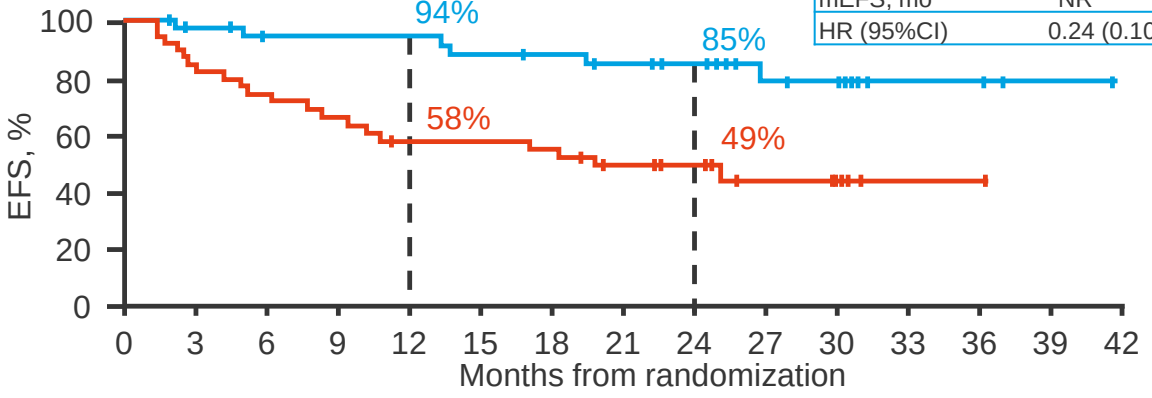


No. at risk

Nivo + chemo	51	43	39	36	35	34	33	28	24	12	9	4	1	0	0
Chemo	47	40	33	29	25	21	18	17	15	10	10	3	3	1	0

PD-L1 ≥50%

	Nivo + chemo (n=38)	Chemo (n=42)
mEFS, mo	NR	19.6
HR (95%CI)	0.24 (0.10, 0.61)	



Nivo + chemo	38	33	30	30	30	28	27	25	23	12	10	3	2	1	0
Chemo	42	31	27	24	20	20	19	15	12	6	5	5	5	0	0

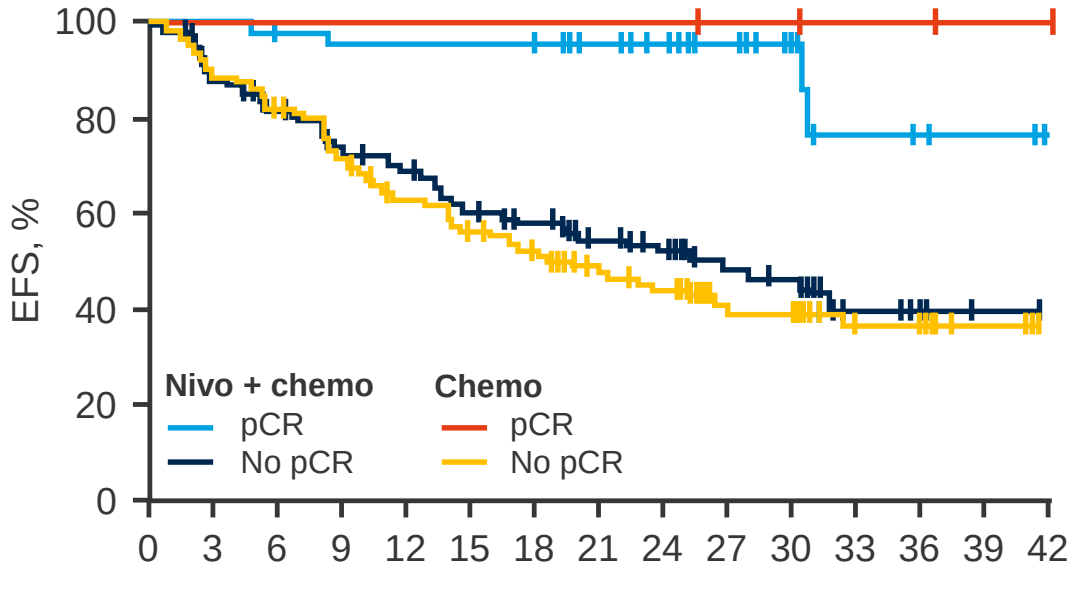
Girard N, et al. AACR; 2022. Abstract nr CT012

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Key results**

Event-free survival by pCR status

	Nivo + chemo		Chemo	
	pCR	No pCR	pCR	No pCR
mEFS, mo	NR	26.6	NR	18.4
HR (95%CI)	0.13 (0.05, 0.37)		Not computed	

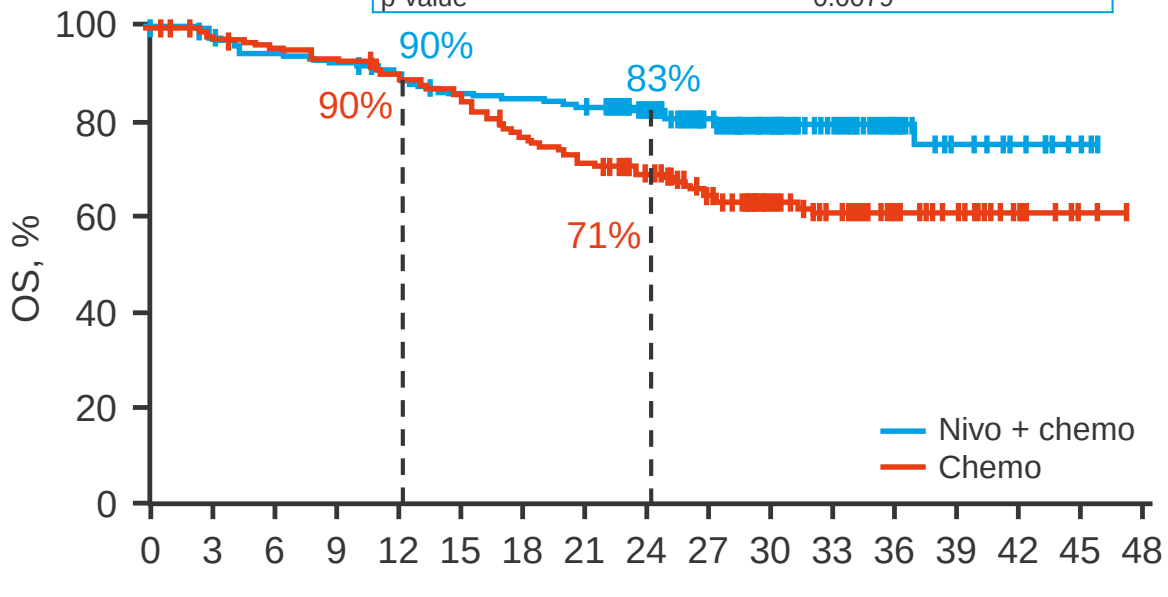


No. at risk

Nivo + chemo	pCR	43	43	41	40	40	40	40	35	32	19	14	6	3	2	0
	No pCR	136	108	95	84	78	67	62	52	42	22	20	7	3	1	0
Chemo	pCR	4	4	4	4	4	4	4	4	4	3	2	2	2	1	0
	No pCR	175	140	122	105	90	79	71	57	48	23	22	11	9	3	0

Overall survival

	Nivo + chemo (n=179)	Chemo (n=179)
mOS, mo	NR	NR
HR (99.67%CI)	0.57 (0.30, 1.07)	
p-value	0.0079	



Nivo + chemo	179	176	166	163	156	148	146	143	122	101	72	48	26	16	7	3	0
Chemo	179	172	165	161	154	148	133	123	108	80	59	41	24	16	7	2	0

Girard N, et al. AACR; 2022. Abstract nr CT012

CT012: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer (NSCLC): Event-free survival (EFS) results from the phase 3 CheckMate 816 trial – Girard N, et al

- **Key results (cont.)**

Grade 3–4 AEs, %	Nivolumab + chemotherapy (n=176)	Chemotherapy (n=176)
Any	41	44
TRAEs	34	37
AE led to discontinuation	6	4
TRAE led to discontinuation	6	3
SAEs	11	10
Treatment-related SAEs	8	8
Surgery-related AEs	11	15
TRAE led to death	0	2

- **Conclusions**
  - In patients with resectable NSCLC, neoadjuvant nivolumab + chemotherapy demonstrated a significant improvement in EFS compared with chemotherapy alone and had a safety profile similar to previous reports

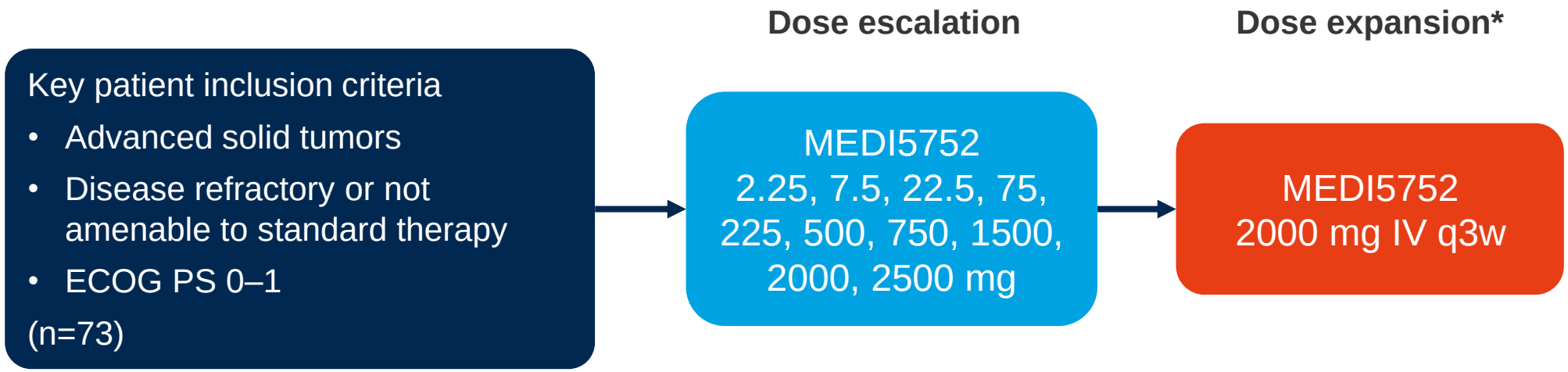
Girard N, et al. AACR; 2022. Abstract nr CT012

Advanced NSCLC
Not radically treatable stage III and stage IV

Immunotherapy strategies

CT016: MEDI5752, a novel PD-1/CTLA-4 bispecific checkpoint inhibitor for advanced solid tumors: First-in-human study – Tran B, et al

- **Study objective**
  - To evaluate the efficacy and safety of MEDI5752, a PD-1/CTLA-4 bispecific checkpoint inhibitor, in patients with advanced solid tumors including NSCLC and renal cell carcinoma (RCC)



Primary endpoint

- Safety

Secondary endpoints

- Antitumor activity, PK

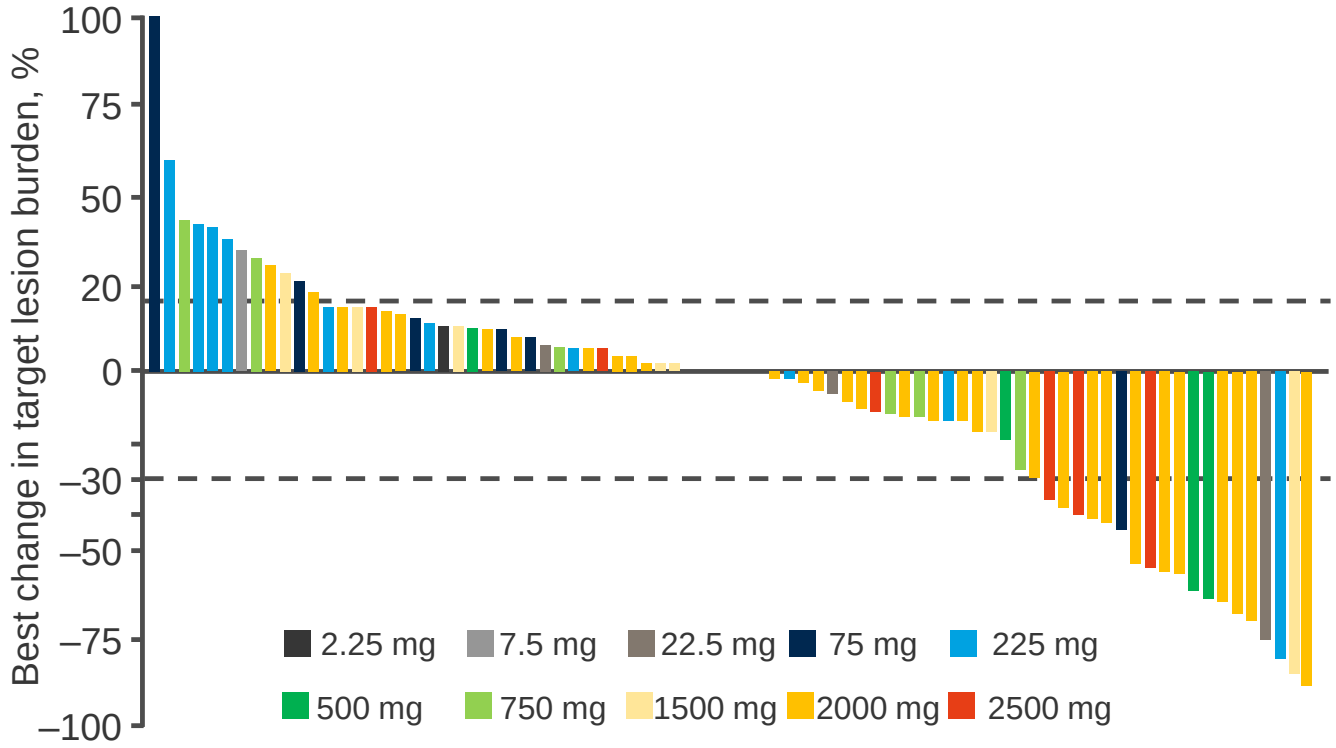
*IO naïve expansion cohort and disease-specific expansions for 1L NSCLC and 1L RCC

Tran B, et al. AACR; 2022. Abstract nr CT016

CT016: MEDI5752, a novel PD-1/CTLA-4 bispecific checkpoint inhibitor for advanced solid tumors: First-in-human study – Tran B, et al

- **Key results**

	Total (n=86)
ORR, n (%) [95%CI]	17 (19.8) [12.0, 29.8]
BOR, n (%)	
CR	1 (1.2)
PR	16 (18.6)
SD	29 (33.7)
PD	32 (37.2)
NE	8 (9.3)
DCR, n (%) [95%CI]	46 (53.5) [42.2, 64.3]



Objective responses with MEDI5752 2000 mg observed in
- 2 patients with NSCLC, both PD-L1 <1%
- 1 patient with mesothelioma
- 1 patient with thymic carcinoma

CT016: MEDI5752, a novel PD-1/CTLA-4 bispecific checkpoint inhibitor for advanced solid tumors: First-in-human study – Tran B, et al

- **Key results (cont.)**

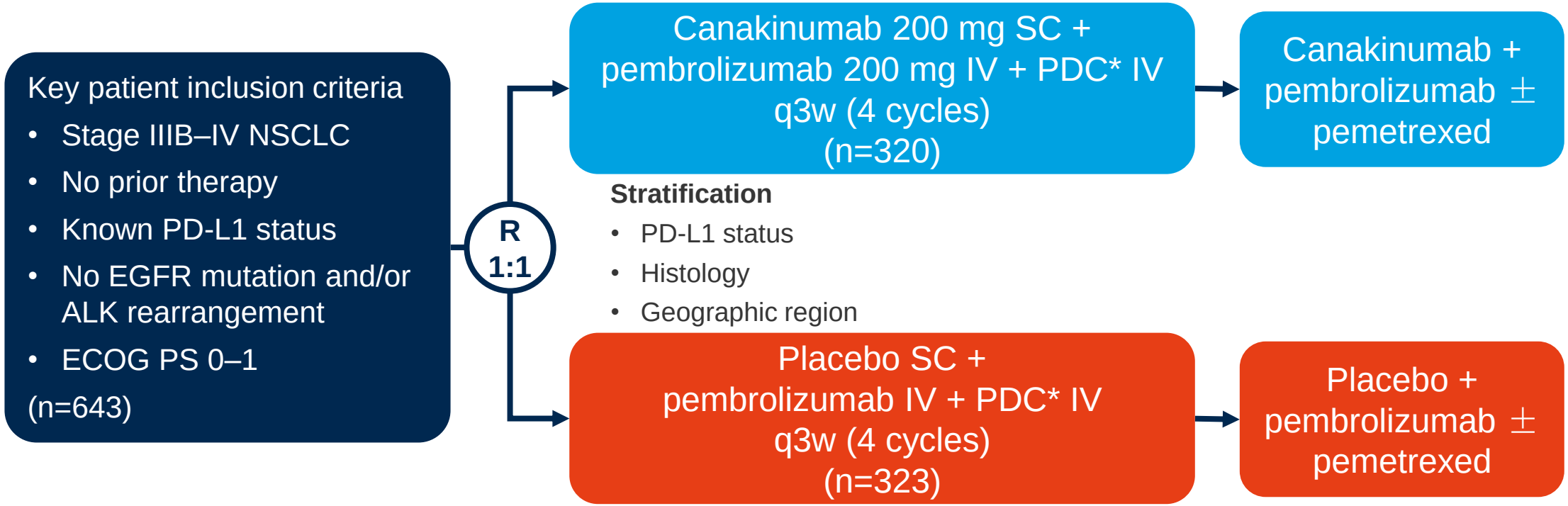
	Total (n=86)	
AEs, n (%)	Any grade	Grade 3–4
TRAE	73 (85)	33 (38.4)
TRAE led to discontinuation	27 (31)	
Death	3 (4)	
Dose-limiting toxicities	2	
AEs of special interest		
Any	69 (80)	32 (37)
Dermatitis/rash	48 (56)	5 (6)
Hepatic events	23 (27)	15 (17)
Hypothyroidism	23 (27)	0
Infusion-related reactions	14 (16)	0
Diarrhea/colitis	9 (11)	2 (2)

- **Conclusions**
  - In patients with IO-naïve advanced solid tumors, MEDI5752 demonstrated deep and durable responses with doses <1500 mg being better tolerated than doses ≥1500 mg

Tran B, et al. AACR; 2022. Abstract nr CT016

CT037: Canakinumab in combination with first-line (1L) pembrolizumab plus chemotherapy for advanced non-small cell lung cancer (aNSCLC): Results from the CANOPY-1 phase 3 trial – Tan DS, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L pembrolizumab + platinum-based doublet chemotherapy (PDC)* in patients with locally advanced or metastatic NSCLC in the phase 3 CANOPY-1 study



Primary endpoints

- PFS, OS

Secondary endpoints

- ORR, DCR, DoR, PROs, safety

*For nonsquamous: carboplatin AUC 5 mg/mL*min q3w or cisplatin 75 mg/m^2 q3w and pemetrexed 500 mg/m^2 q3w; for squamous: carboplatin 6 mg/mL*min q3w and paclitaxel 200 mg/m^2 q3w or nab-paclitaxel 100 mg/m^2 q3w

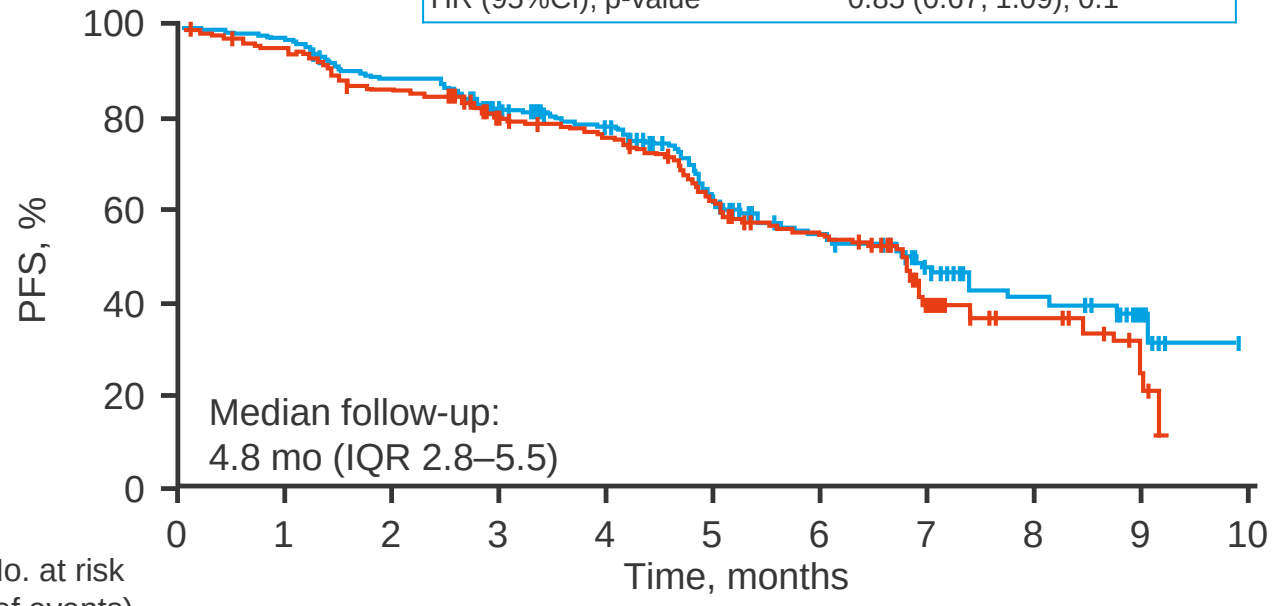
Tan DS, et al. AACR; 2022. Abstract nr CT037

CT037: Canakinumab in combination with first-line (1L) pembrolizumab plus chemotherapy for advanced non-small cell lung cancer (aNSCLC): Results from the CANOPY-1 phase 3 trial – Tan DS, et al

- **Key results**

Progression-free survival

	Canakinumab (n=320)	Placebo (n=323)
mPFS, mo	6.8	6.8
HR (95%CI); p-value	0.85 (0.67, 1.09); 0.1	

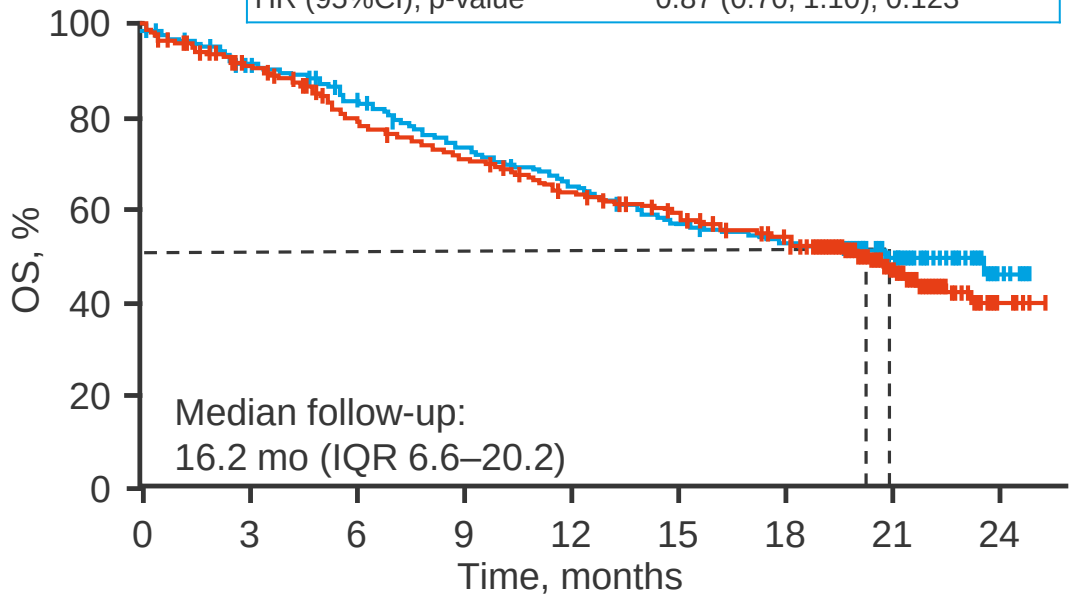


No. at risk (no. of events)											
Canakinumab	320 (0)	309 (7)	277 (35)	233 (55)	210 (65)	98 (103)	75 (111)	37 (120)	23 (124)	13 (126)	0 (127)
Placebo	323 (0)	299 (16)	268 (43)	223 (61)	207 (73)	98 (107)	75 (118)	37 (136)	24 (138)	9 (141)	0 (145)

Primary endpoints not met

Overall survival

	Canakinumab (n=320)	Placebo (n=323)
mOS, mo	20.8	20.2
HR (95%CI); p-value	0.87 (0.70, 1.10); 0.123	



320 (0)	287 (24)	254 (48)	217 (79)	193 (102)	165 (126)	148 (138)	55 (146)	9 (147)
323 (0)	285 (28)	242 (64)	213 (89)	188 (112)	173 (125)	153 (141)	64 (153)	7 (159)

Tan DS, et al. AACR; 2022. Abstract nr CT037

CT037: Canakinumab in combination with first-line (1L) pembrolizumab plus chemotherapy for advanced non-small cell lung cancer (aNSCLC): Results from the CANOPY-1 phase 3 trial – Tan DS, et al

- **Key results (cont.)**

Responses	Canakinumab + pembrolizumab + PDC (n=320)	Placebo + pembrolizumab + PDC (n=323)
ORR, % (95%CI)	45.6 (40.1, 51.3)	45.5 (40.0, 51.1)
BOR, n (%)		
CR	1 (0.3)	3 (0.9)
PR	145 (45.3)	144 (4.6)
SD	132 (41.3)	127 (39.3)
PD	23 (7.2)	25 (7.7)
NE	19 (5.9)	24 (7.4)
DCR, % (95%CI)	86.9 (82.7, 90.4)	84.8 (80.4, 88.6)
DoR, no. of events	76	79
mDoR, mo (95%CI)	14.3 (10.4, NE)	13.6 (10.3, NE)

Grade 3–4 AEs, %	Canakinumab + pembrolizumab + PDC (n=320)	Placebo + pembrolizumab + PDC (n=323)
Neutropenia	24.4	16.8
Anemia	16.3	20.5
Neutrophil count decreased	13.4	11.5
Dyspnea	5.3	5.0
ALT increased	4.7	3.1
Nausea	2.2	1.6
Diarrhea	2.2	4.0
Asthenia	1.6	3.7
Appetite decreased	1.6	1.2
Constipation	0	0.3

- **Conclusions**
  - In patients with advanced NSCLC, combining canakinumab with pembrolizumab + platinum-doublet chemotherapy did not provide any additional improvements in survival in the 1L setting and there were no unexpected safety findings

Tan DS, et al. AACR; 2022. Abstract nr CT037

Advanced NSCLC
Not radically treatable stage III and stage IV

Targeted therapies

ND02: MRTX0902: A SOS1 inhibitor for therapeutic intervention of KRAS-driven cancers – Ketcham JM, et al

- **Study objective**
  - To evaluate the in vitro and in vivo efficacy of MRTX0902, a SOS1 inhibitor, for treating patients with KRAS-driven cancers

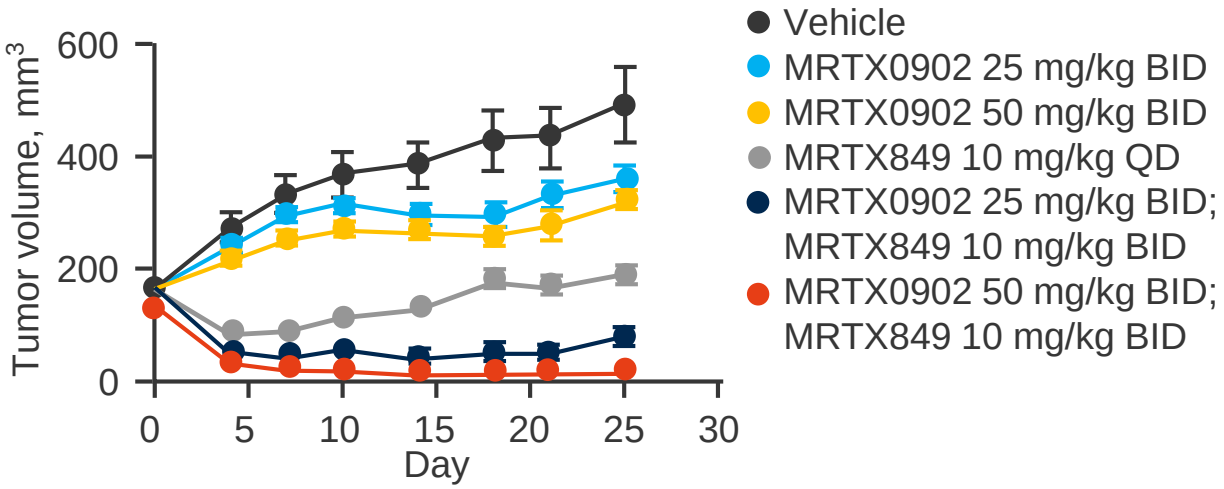
- **Methods**
  - A structure-enabled approach was used to design a novel series of phthalazine-based SOS1 inhibitors that can bind to the SOS1:KRAS interface to disrupt protein-protein interactions
  - The activity of MRTX0902 was assessed in preclinical species and NSCLC and CRC PDX models

Presented by Dr Jacob R Haling
Ketcham JM, et al. AACR; 2022. Abstract nr ND02

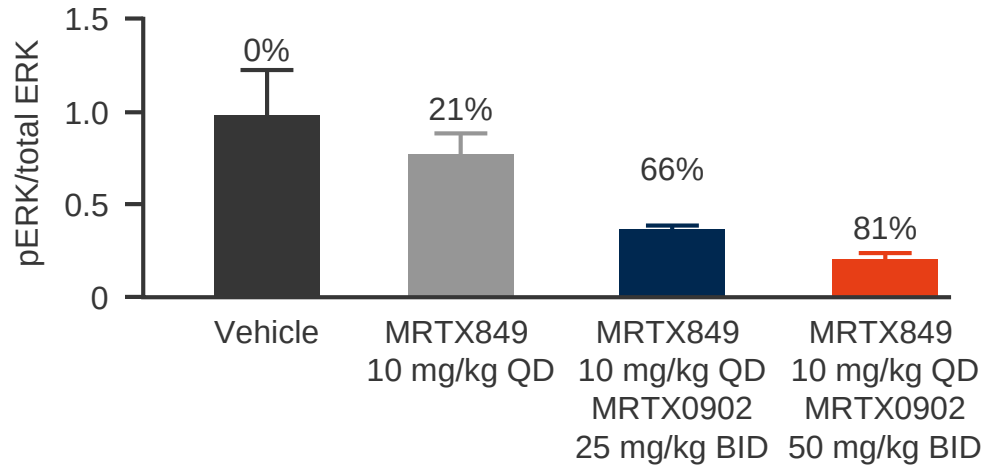
ND02: MRTX0902: A SOS1 inhibitor for therapeutic intervention of KRAS-driven cancers – Ketcham JM, et al

- **Key results**

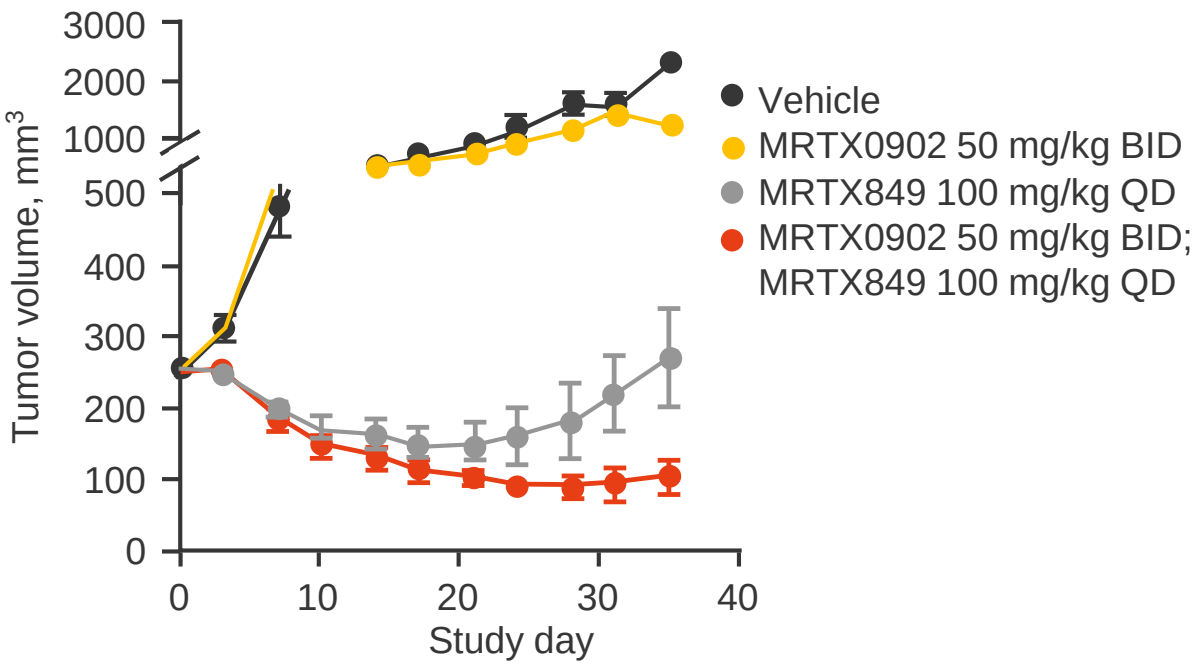
MIA PaCa-2 (KRAS G12C)



pERK modulation in MIA PaCa-2 (4 hours post-dose)



LU11692 (NSCLC PDX model)



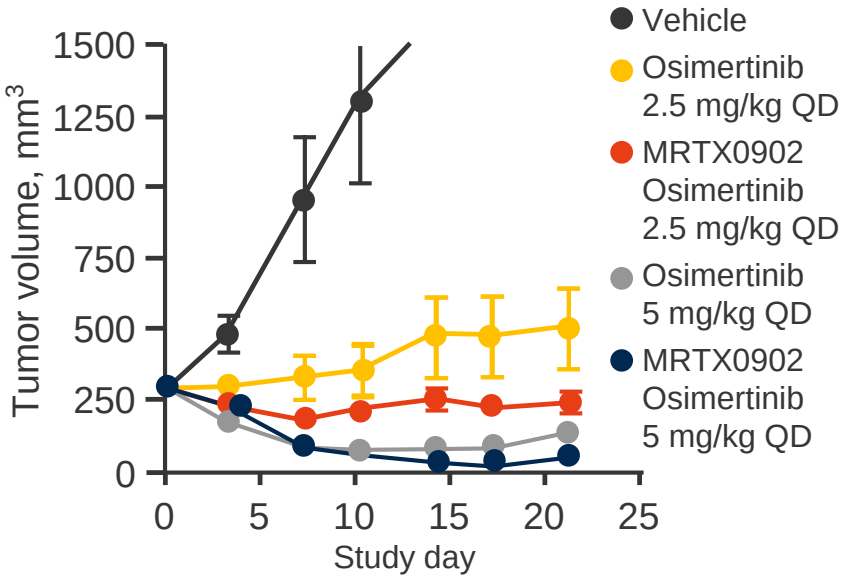
Ketcham JM, et al. AACR; 2022. Abstract nr ND02

ND02: MRTX0902: A SOS1 inhibitor for therapeutic intervention of KRAS-driven cancers – Ketcham JM, et al

- **Key results (cont.)**

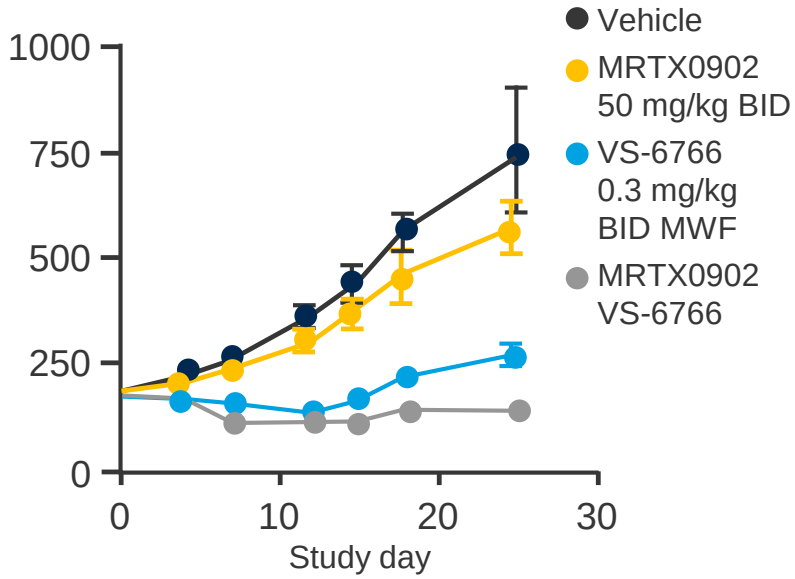
SOS1 + EGFR inhibitors

NCI-H1975 (EGFR L858R/T790M)



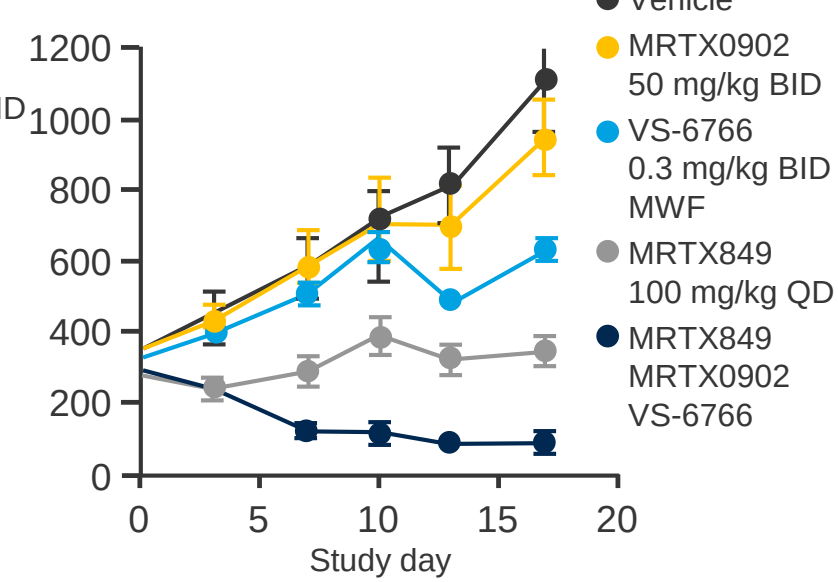
SOS1 + dual RAF/MEKc inhibitors

LN229 (PTPN11 A72S)



SOS1 + dual RAF/MEKc + KRAS G12C inhibitors

H2122 (KRAS G12C)

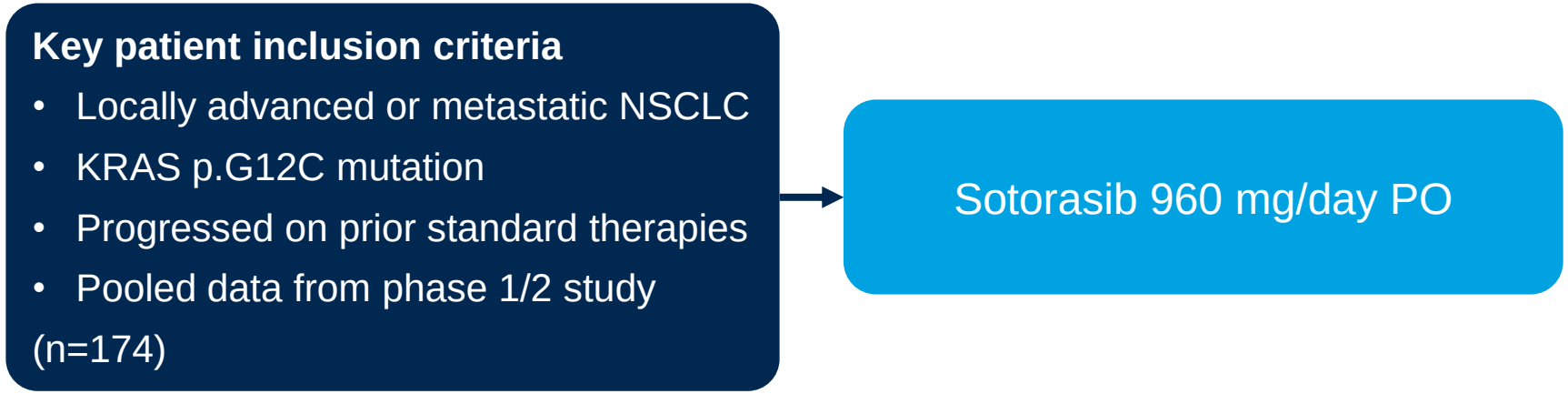


- **Conclusions**
  - In preclinical species, MRTX0902 demonstrated encouraging potency and selectively, and its antitumor response, including depth and durability, was enhanced when combined with MRTX849 in KRAS G12C tumor models

Ketcham JM, et al. AACR; 2022. Abstract nr ND02

CT008: Long-term outcomes with sotorasib in pretreated KRASp.G12C-mutated NSCLC: 2-year analysis of CodeBreaK100 – Dy GK, et al

- **Study objective**
  - To evaluate the long-term efficacy and safety of sotorasib in previously treated patients with KRAS G12C-mutated NSCLC in the CodeBreaK100 study



Primary endpoint

- ORR (RECIST v1.1, ICR)

Secondary endpoints

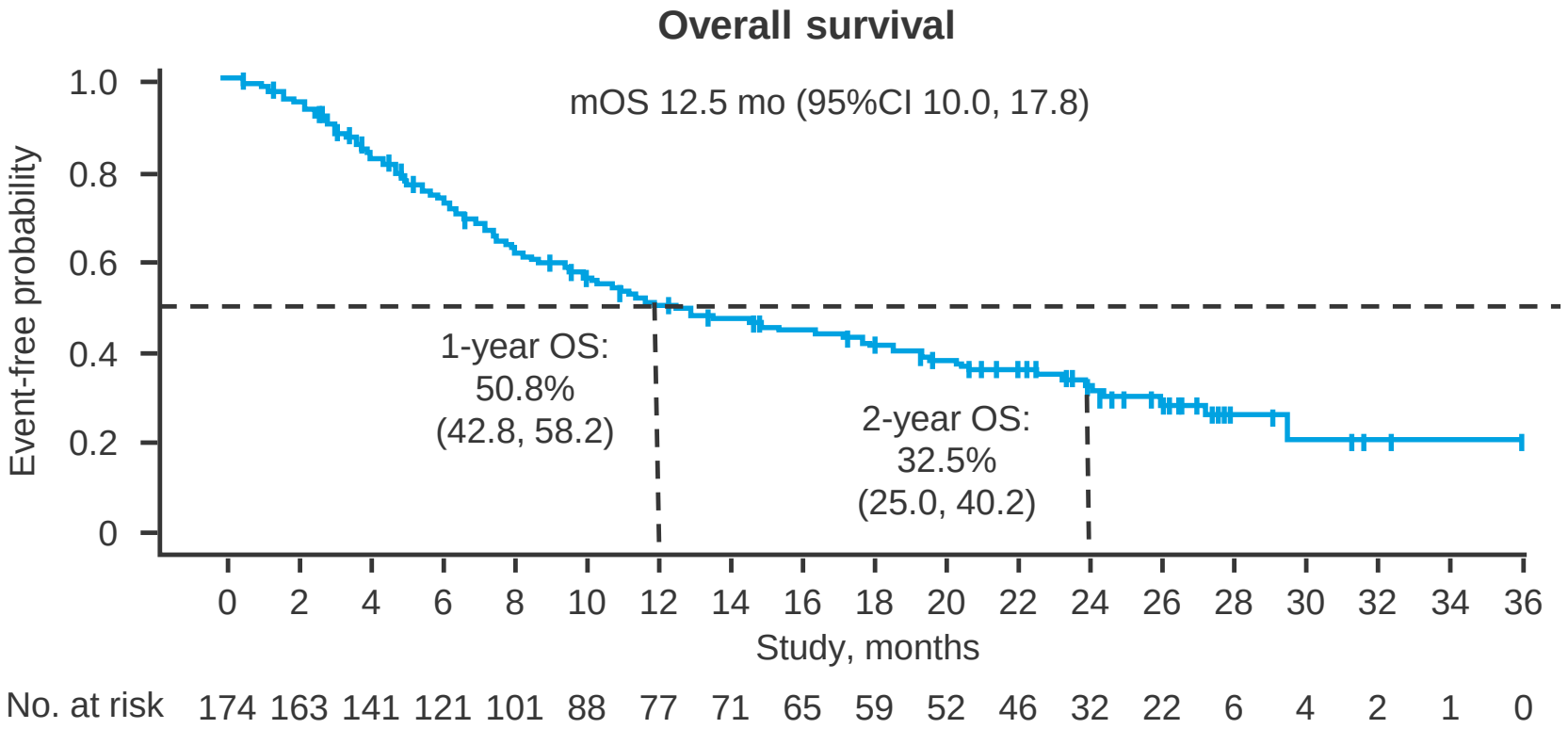
- DoR, DCR, TTR, PFS, OS, safety

Dy GK, et al. AACR; 2022. Abstract nr CT008

CT008: Long-term outcomes with sotorasib in pretreated KRASp.G12C-mutated NSCLC: 2-year analysis of CodeBreaK100 – Dy GK, et al

- **Key results**

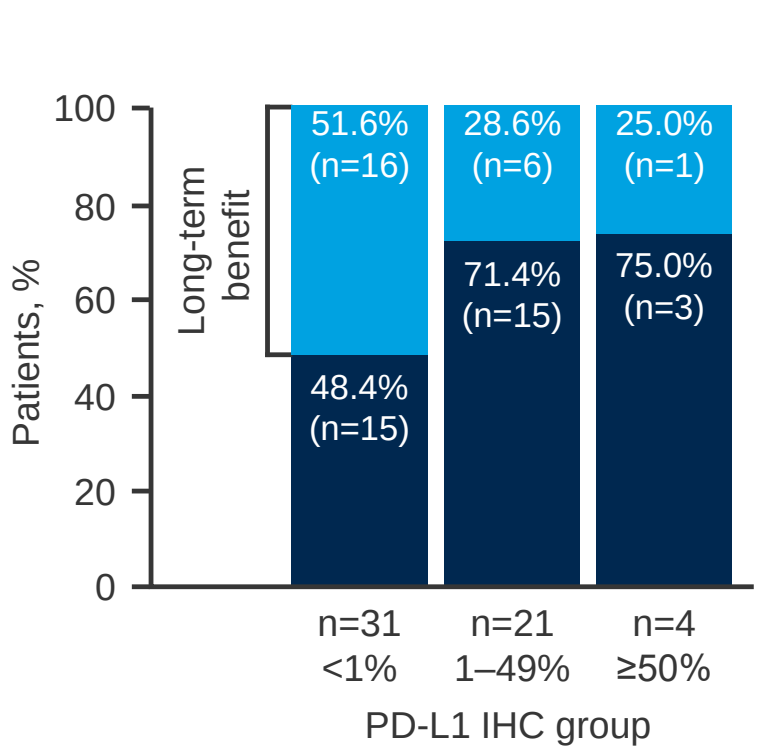
Response	n=172
ORR, % (95%CI)	40.7 (33.3, 48.4)
BOR, n (%)	
CR	5 (2.9)
PR	65 (37.8)
SD	74 (43.0)
PD	23 (13.4)
NE	5 (2.9)
DCR, % (95%CI)	83.7 (77.3, 88.9)
mPFS, mo (95%CI)	6.3 (5.3, 8.2)
mDoR, mo (95%CI)	12.3 (7.1, 15.0)

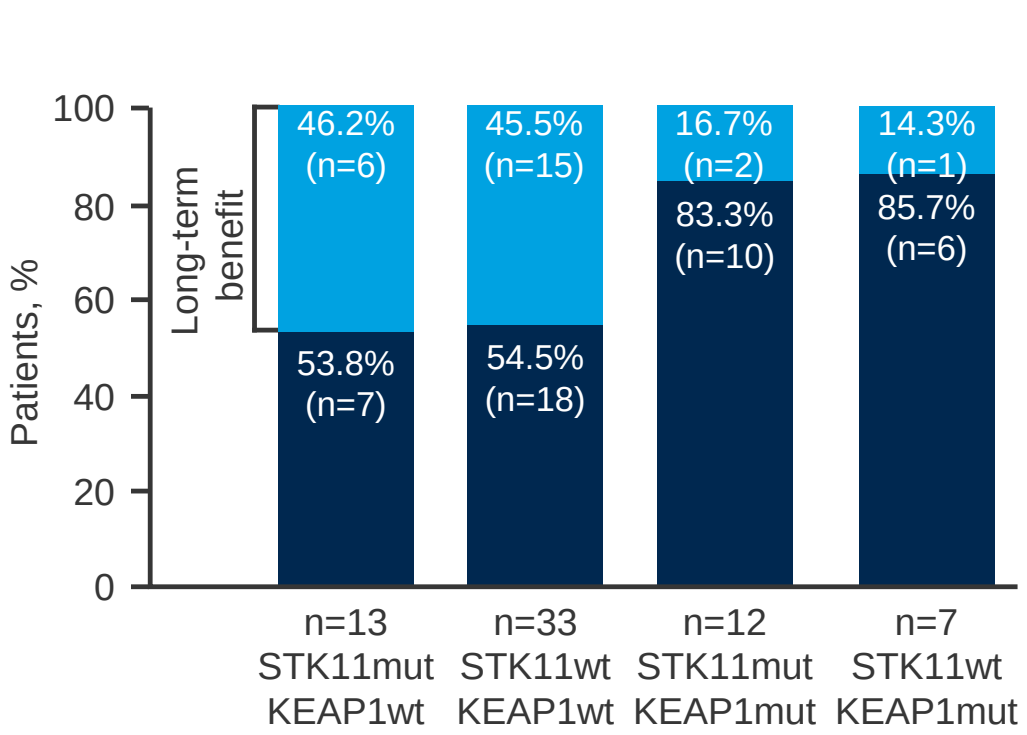


Dy GK, et al. AACR; 2022. Abstract nr CT008

CT008: Long-term outcomes with sotorasib in pretreated KRASp.G12C-mutated NSCLC: 2-year analysis of CodeBreaK100 – Dy GK, et al

- **Key results**
  - Long-term benefit was seen regardless of PD-L1 or KRAS G12C expression
  - Patients with long-term benefit had lower plasma ctDNA at baseline and these levels correlated with tumor burden





Dy GK, et al. AACR; 2022. Abstract nr CT008

CT008: Long-term outcomes with sotorasib in pretreated KRASp.G12C-mutated NSCLC: 2-year analysis of CodeBreaK100 – Dy GK, et al

- **Key results (cont.)**

TRAEs, %	Overall (n=174)	Onset after 1 year (n=45)
Any	70	24
Grade 2	20	9
Grade 3	20	2
Grade 4	1	0
Led to treatment modification	22	2
Led to discontinuation	6	0

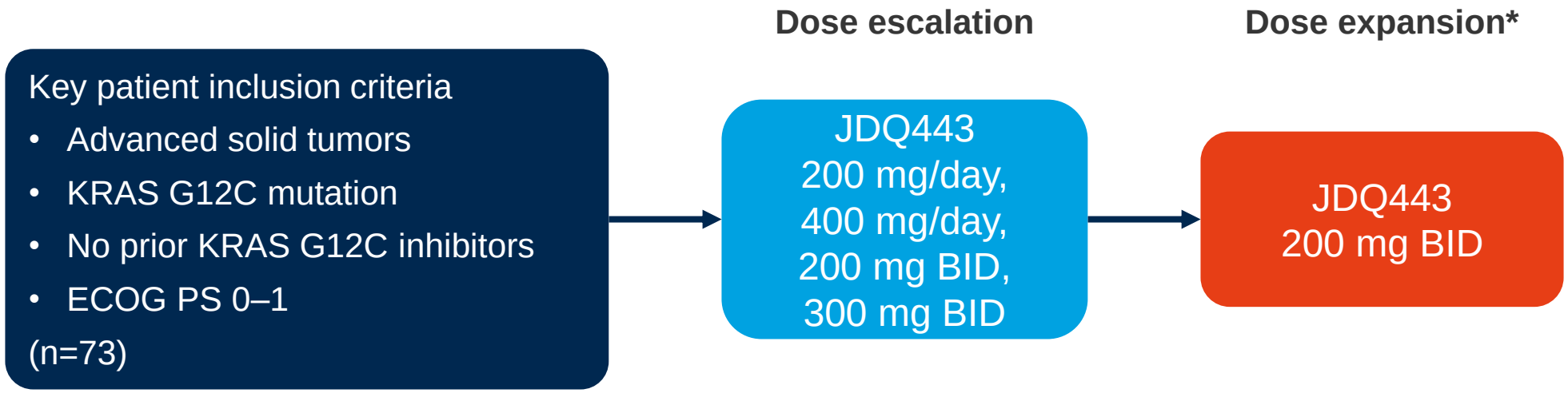
TRAEs, %	Overall (n=174)	Onset after 1 year (n=45)
Diarrhea	31	0
ALT increased	18	0
AST increased	18	0
Nausea	16	2
Fatigue	12	4
ALP increased	8	0
Vomiting	7	0

- **Conclusions**
  - In previously treated patients with KRAS G12C-mutated NSCLC, sotorasib continued to provide durable efficacy with one quarter of patients having long-term clinical benefit (PFS ≥12 months) and with a safety profile similar to previous findings

Dy GK, et al. AACR; 2022. Abstract nr CT008

CT033: KontRASt-01: A phase Ib/II, dose-escalation study of JDQ443 in patients (pts) with advanced, KRAS G12C-mutated solid tumors – Tan DS, et al

- **Study objective**
  - To evaluate the safety and efficacy of JDQ443, a KRAS G12C inhibitor, in patients with advanced KRAS G12C-mutated solid tumors in the phase 1b/2 KontRASt-01 study



Primary endpoint

- Safety

Secondary endpoints

- Antitumor activity, PK

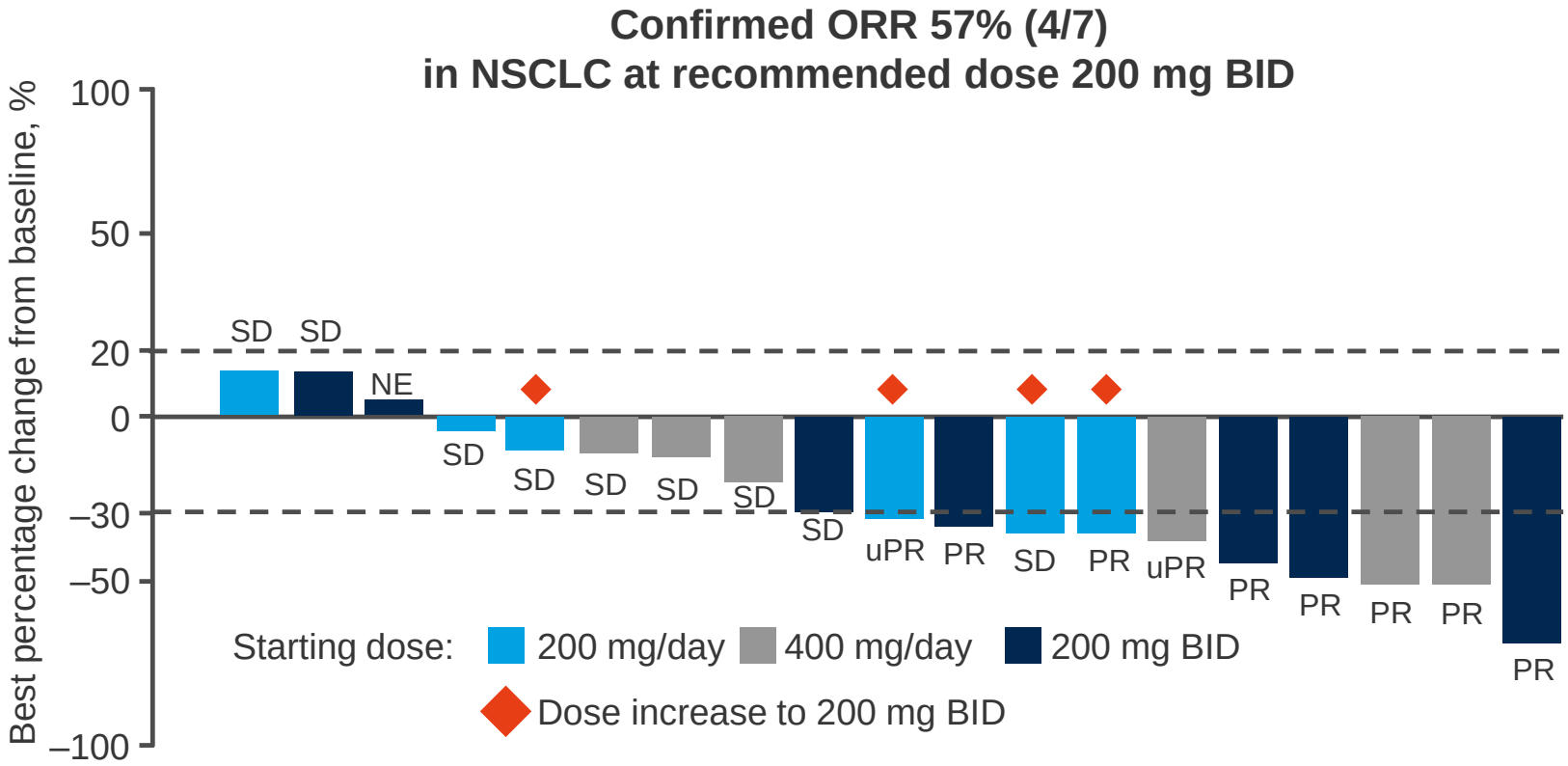
*In previously treated patients with NSCLC or CRC harbouring KRAS G12C mutations

Tan DS, et al. AACR; 2022. Abstract nr CT033

CT033: KontRASt-01: A phase Ib/II, dose-escalation study of JDQ443 in patients (pts) with advanced, KRAS G12C-mutated solid tumors – Tan DS, et al

- **Key results**

BoR, n (%)	Patients with NSCLC (n=20)
PR (confirmed)	7 (35)
SD	11 (55)
PD	0
NE	2 (10)
ORR (confirmed and unconfirmed)	9 (45)
ORR (confirmed)	7 (35)



Tan DS, et al. AACR; 2022. Abstract nr CT033

CT033: KontRASt-01: A phase Ib/II, dose-escalation study of JDQ443 in patients (pts) with advanced, KRAS G12C-mutated solid tumors – Tan DS, et al

- **Key results (cont.)**

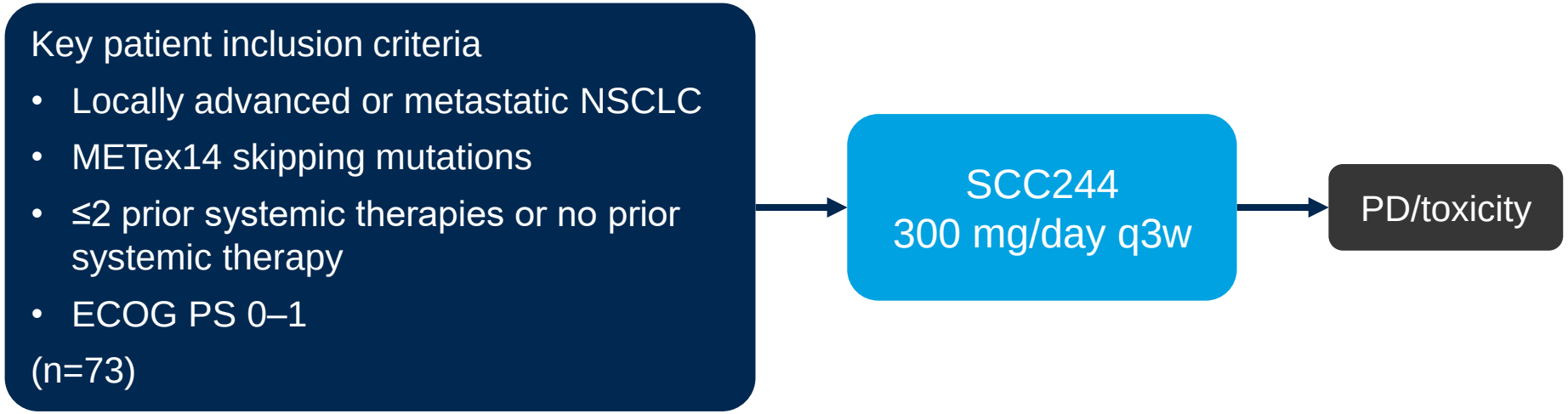
Grade ≥3 TRAEs, n (%)	JDQ443 200 mg BID (n=11)	JDQ443 all patients (n=39)
Any	0	5 (12.8)
Photosensitivity reaction	0	2 (5.1)
Fatigue	0	1 (2.6)
Neutropenia	0	1 (2.6)

- **Conclusions**
  - In patients with advanced NSCLC harboring KRAS G12C mutations, JDQ443 demonstrated encouraging antitumor activity and had an acceptable safety profile

Tan DS, et al. AACR; 2022. Abstract nr CT033

CT034: Phase II study of SCC244 in NSCLC patients harboring MET exon 14 skipping (METex14) mutations (GLORY study) – Lu S, et al

- **Study objective**
  - To evaluate the efficacy and safety of SCC244, a MET inhibitor, in patients with NSCLC harboring MET exon 14 skipping mutations in the phase 2 GLORY study



Primary endpoint

- ORR (BIRC, RECIST v1.1.)

Secondary endpoints

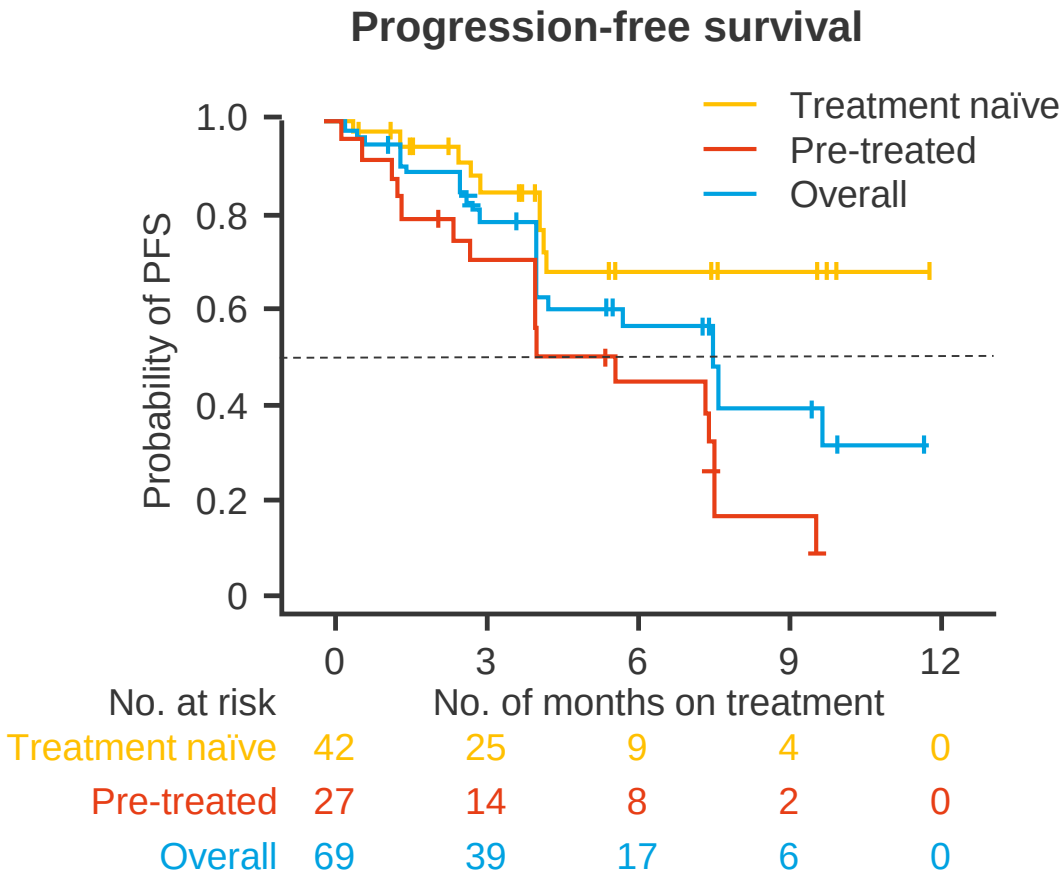
- DoR, DCR, TTR, PFS, OS, safety

Lu S, et al. AACR; 2022. Abstract nr CT034

CT034: Phase II study of SCC244 in NSCLC patients harboring MET exon 14 skipping (METex14) mutations (GLORY study) – Lu S, et al

- **Key results**

Efficacy analysis set	Treatment-naïve (n=42)	Previously treated (n=27)	All (n=69)
ORR, % (95%CI)	66.7 (50.5, 80.4)	51.9 (31.9, 71.3)	60.9 (48.4, 72.4)
DCR, % (95%CI)	88.1 (74.4, 96.0)	74.1 (53.7, 88.9)	82.6 (71.6, 90.7)
mDoR, mo (95%CI)	NE (NE, NE)	5.1 (2.8, 8.2)	8.2 (4.8, NE)
PFS events, n (%)	9 (21.4)	17 (63.0)	26 (37.7)
mPFS, mo (95%CI)	NE (4.3, NE)	5.7 (2.8, 7.6)	7.6 (4.2, NE)



Lu S, et al. AACR; 2022. Abstract nr CT034

CT034: Phase II study of SCC244 in NSCLC patients harboring MET exon 14 skipping (METex14) mutations (GLORY study) – Lu S, et al

- **Key results (cont.)**

TRAEs, n (%)	All (n=73)
Any	71 (97.3)
Grade ≥3	32 (43.8)
Serious	13 (17.8)
Led to dose interruption	18 (24.7)
Led to dose reduction	21 (28.8)
Led to discontinuation	5 (6.8)

Grade ≥3 TRAEs, n (%)	All (n=73)
Peripheral edema	14 (19.2)
Neutropenia	3 (4.1)
Headache	2 (2.7)
Rash	2 (2.7)
ALT increased	1 (1.4)
Vomiting	1 (1.4)
AST increased	1 (1.4)
Facial edema	1 (1.4)
Hypokalemia	1 (1.4)
Leukopenia	1 (1.4)

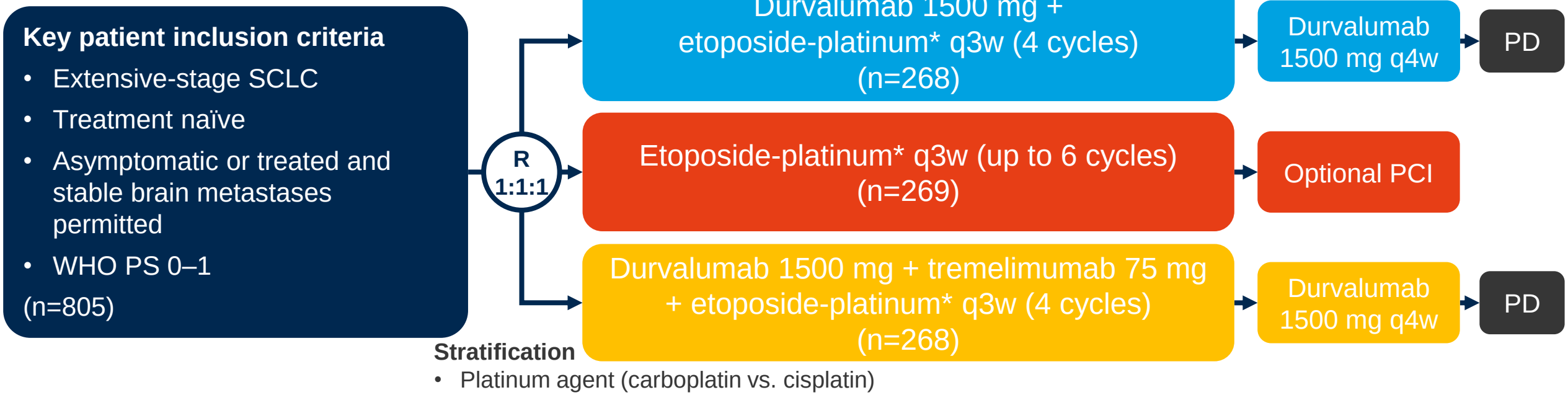
- **Conclusions**
  - In patients with locally advanced or metastatic NSCLC harboring METex14 skipping mutations, SCC244 demonstrated promising efficacy and had a manageable safety profile

Other malignancies

SCLC, mesothelioma and thymic epithelial tumors

CT024: Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN – Xie M, et al

- **Study objective**
  - To evaluate the concordance between two RNAseq-based methods[1,2] for SCLC subtyping and the association of subtypes on survival in patients with extensive-stage SCLC treated with durvalumab + etoposide-platinum in the CASPIAN study



Primary endpoint

- OS

Secondary endpoints

- PFS, ORR, PROs, safety, biomarker analysis†

*Etoposide 80–100 mg/m^2 + carboplatin AUC5–6 or cisplatin 75–80 mg/m^2;†including tissue TMB and PD-L1

1. Rudin et al. *Nat Rev Cancer* 2019;19:289–97; 2. Gay et al. *Cancer Cell* 2021;39:346–60

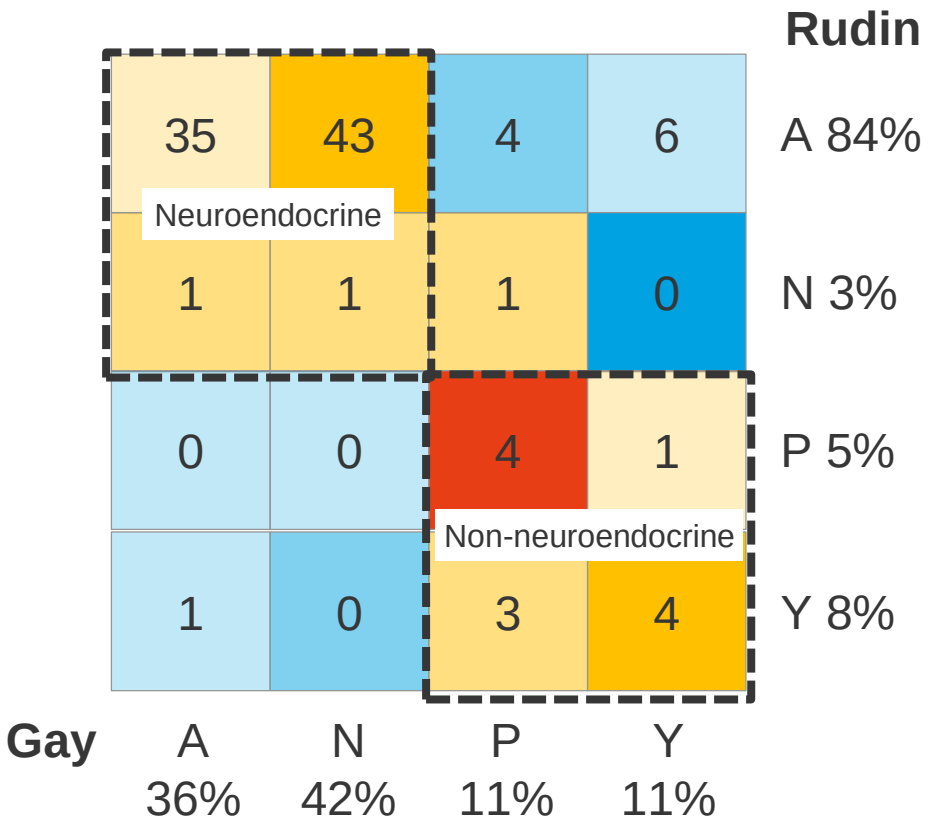
Presented by Dr Yashaswi Shrestha

Xie M, et al. AACR; 2022. Abstract nr CT024

CT024: Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN – Xie M, et al

- **Key results**

SCLC molecular subtype prevalence



OS by molecular subtype

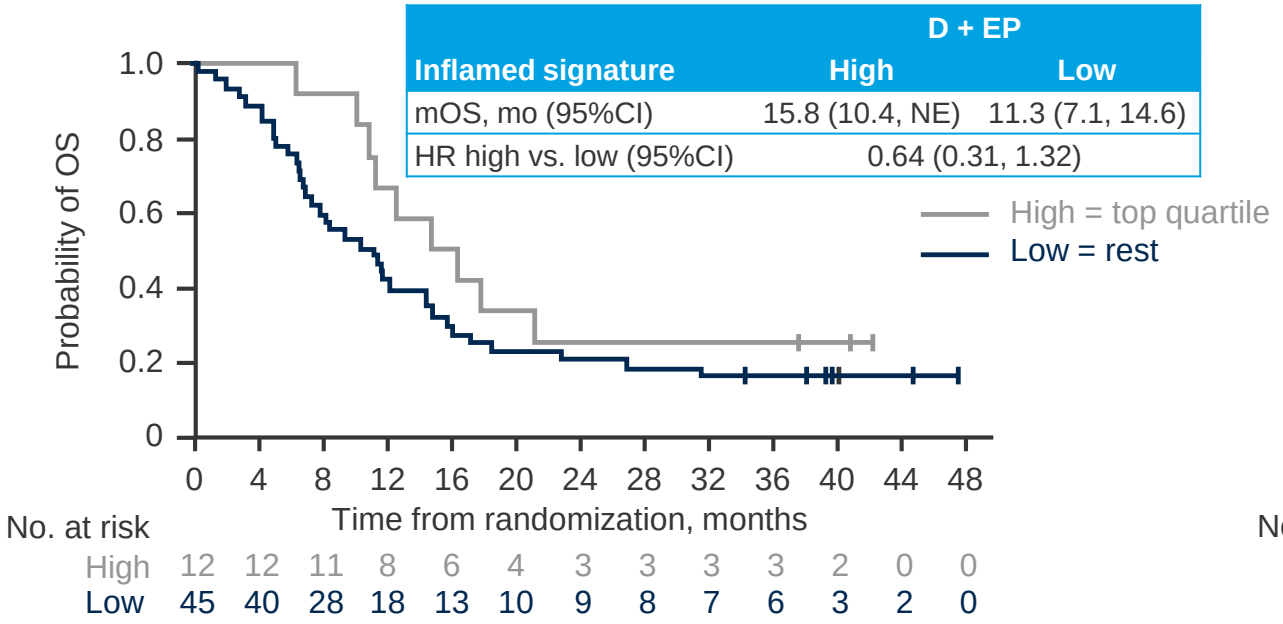
	n	D + EP mOS, mo (95%CI)	n	EP mOS, mo (95%CI)
ITT	268	12.9 (11.3, 14.7)	269	10.5 (9.3, 11.2)
BEP	57	11.8 (8.6, 14.9)	47	9.1 (7.7, 11.3)
Rudin et al. method				
ASCL1	50	11.5 (8.4, 14.9)	38	10.7 (8.1, 12.4)
NEUROD1	1	9.5 (NE, NE)	2	7.1 (4.8, NE)
POU2F3	2	4.8 (2.9, NE)	3	6.1 (1.3, NE)
YAP1	4	17.3 (12.8, NE)	4	6.9 (4.5, NE)
Gay et al. method				
ASCL1	21	9.5 (6.1, 14.9)	16	8.3 (3.0, 15.1)
NEUROD1	25	14.6 (8.6, 16.6)	19	10.5 (7.9, 13.6)
POU2F3	5	6.8 (2.9, NE)	7	7.5 (1.3, 10.2)
Inflamed	6	17.6 (11.4, NE)	5	11.3 (6.3, NE)

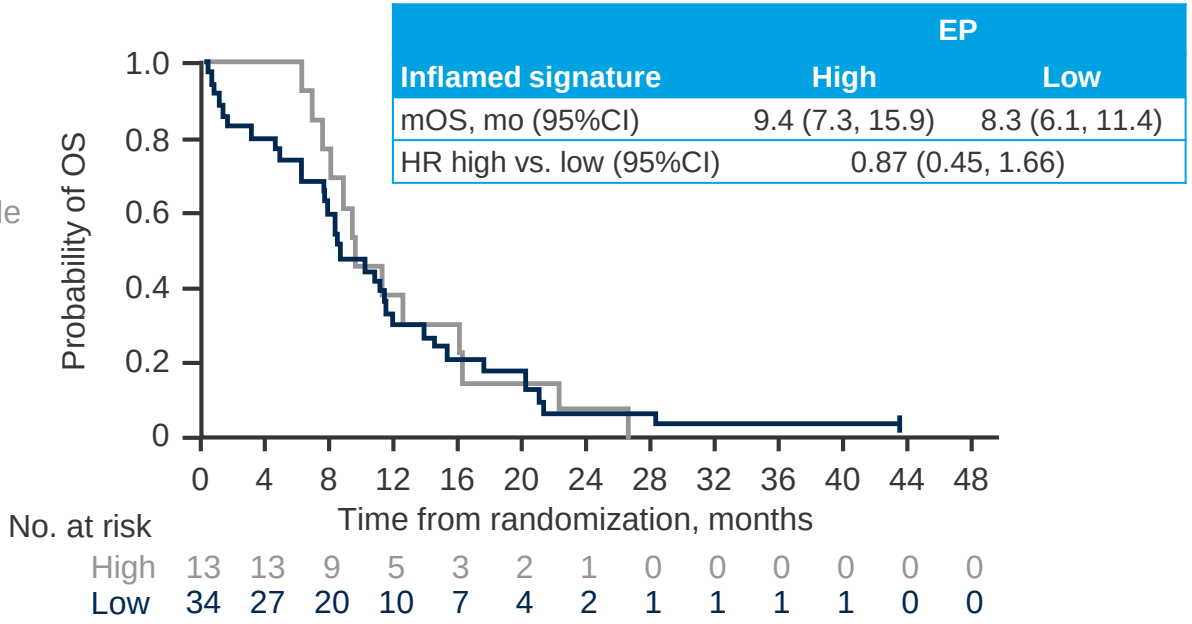
Xie M, et al. AACR; 2022. Abstract nr CT024

CT024: Durvalumab (D) + platinum-etoposide (EP) in 1L extensive-stage small-cell lung cancer (ES-SCLC): Exploratory analysis of SCLC molecular subtypes in CASPIAN – Xie M, et al

- **Key results (cont.)**

OS according to T-cell inflamed signature





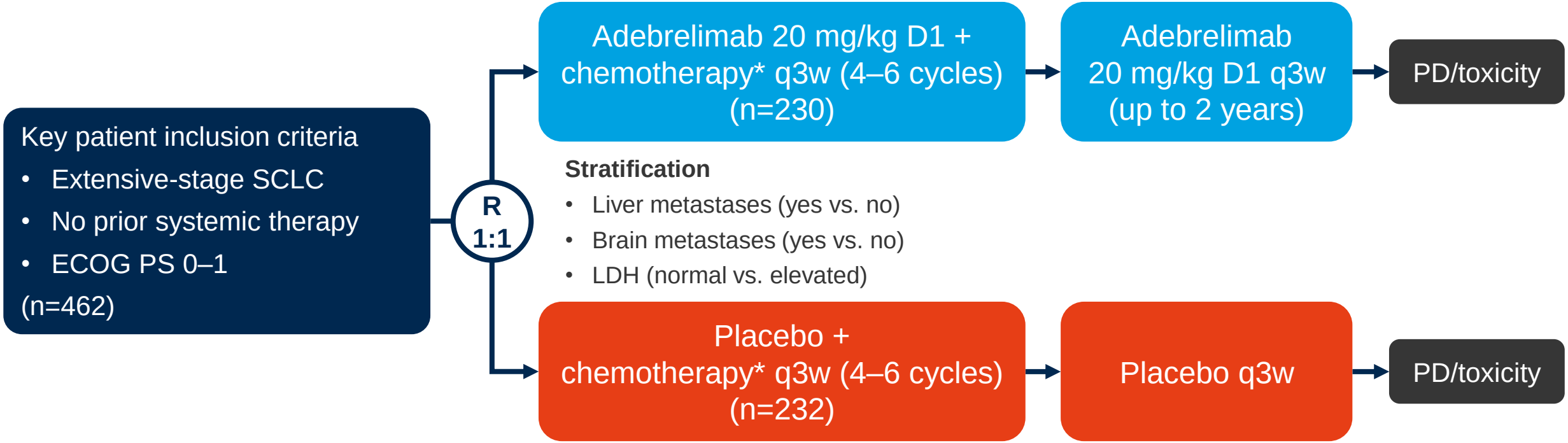
- **Conclusions**
  - In patients with extensive-stage SCLC, there was greater concordance between the two RNAseq-based methods for differentiating between neuroendocrine and non-neuroendocrine subtypes than for distinguishing the four main subtypes
  - Patients with inflamed (Gay et al.[1]) or YAP1 (Rudin et al.[2]) subtype had the longest OS in the durvalumab + etoposide-platinum arm

1. Gay et al. *Cancer Cell* 2021;39:346–60; 2. Rudin et al. *Nat Rev Cancer* 2019;19:289–97

Xie M, et al. AACR; 2022. Abstract nr CT024

CT038: Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage SCLC: A phase 3 trial – Cheng Y, et al

- **Study objective**
  - To evaluate the efficacy and safety of 1L adebrelimab (a fully humanized IgG4 anti-PD-L1 monoclonal antibody) + chemotherapy in patients with extensive-stage SCLC



Primary endpoint

- OS

Secondary endpoints

- PFS, ORR, DoR, DCR, safety

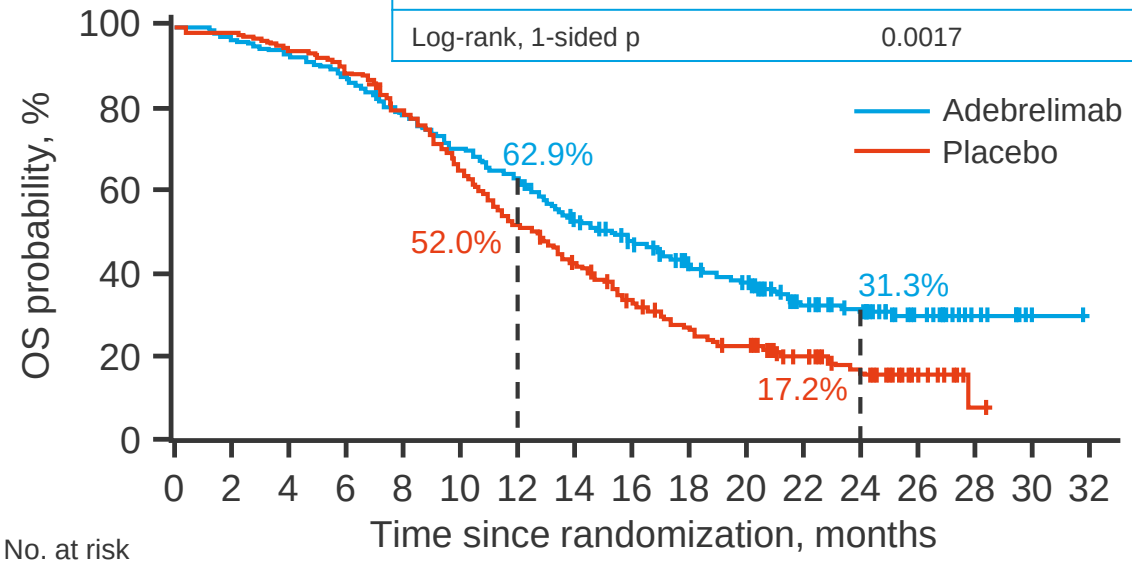
*Carboplatin AUC5 D1 + etoposide 100 mg/m^2 D1–3

CT038: Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage SCLC: A phase 3 trial – Cheng Y, et al

- **Key results**

Overall survival

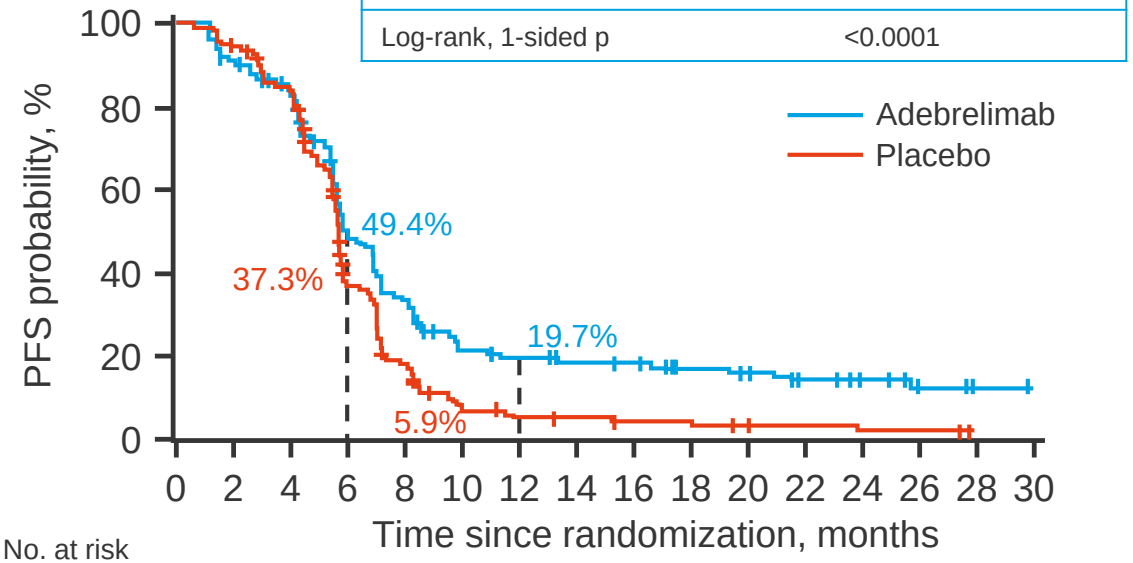
	Adebrelimab + chemotherapy	Placebo + chemotherapy
mOS, mo (95%CI)	15.3 (13.2, 17.5)	12.8 (11.3, 13.7)
HR (95%CI)	0.72 (0.58, 0.90)	
Log-rank, 1-sided p	0.0017	



No. at risk																
Adebrelimab + chemotherapy	230	224	215	202	180	161	144	120	101	84	72	45	37	21	8	3	1
Placebo + chemotherapy	232	229	221	210	185	153	120	98	70	54	44	31	21	10	1	0	

Progression-free survival

	Adebrelimab + chemotherapy	Placebo + chemotherapy
mPFS, mo (95%CI)	5.8 (5.6, 6.9)	5.6 (5.5, 5.7)
HR (95%CI)	0.67 (0.54, 0.83)	
Log-rank, 1-sided p	<0.0001	



No. at risk																
Adebrelimab + chemotherapy	230	200	175	101	67	41	37	33	30	24	21	17	11	5	1	0
Placebo + chemotherapy	232	207	174	72	34	12	9	8	6	5	3	3	2	2	0	

Cheng Y, et al. AACR; 2022. Abstract nr CT038

CT038: Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage SCLC: A phase 3 trial – Cheng Y, et al

- **Key results (cont.)**

	Adebrelimab + chemotherapy (n=230)	Placebo + chemotherapy (n=232)
ORR, % (95%CI)	70.4 (64.1, 76.3)	65.9 (59.5, 72.0)
BOR, n (%)		
CR	7 (3.0)	4 (1.7)
PR	155 (67.4)	149 (64.2)
SD	45 (19.6)	58 (25.0)
PD	16 (7.0)	10 (4.3)
NE	7 (3.0)	11 (4.7)
mDoR, mo (95%CI)	5.6 (4.6, 6.7)	4.6 (4.3, 5.5)
DCR, % (95%CI)	90.0 (85.4, 93.6)	90.9 (86.5, 94.3)

AEs, n (%)	Adebrelimab + chemotherapy (n=230)	Placebo + chemotherapy (n=232)
TRAEs		
Any grade	229 (99.6)	229 (98.7)
Grade 3/4	195 (84.8)	195 (84.1)
Led to discontinuation	12 (5.2)	9 (3.9)
Led to death	2 (0.9)	2 (0.9)
Immune-mediated	64 (27.8)	40 (17.2)

- **Conclusions**
  - In patients with extensive-stage SCLC, adebrelimab + chemotherapy demonstrated significant improvement in survival compared with chemotherapy alone and had a manageable safety profile

Cheng Y, et al. AACR; 2022. Abstract nr CT038