Post-ASCO 2021: Thoracic Oncology Highlights

Prof. Dr. V. Surmont
26 juni 2021

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Outline

- early stage
- unresectable stage III
- metastatic: non-oncogene addicted
- metastatic: oncogene addicted
- SCLC
- take home messages

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Disclosures

- honoraria advisory boards:
  - Astra-Zeneca, Pfizer, MSD, Roche

Early stage NSCLC:

(Neo)adjuvant strategies

IMpower010
Checkmate 816
IMPACT/CTONG1103

Local treatment modalities

VIOLET
STARS

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(neo)adjuvant strategies

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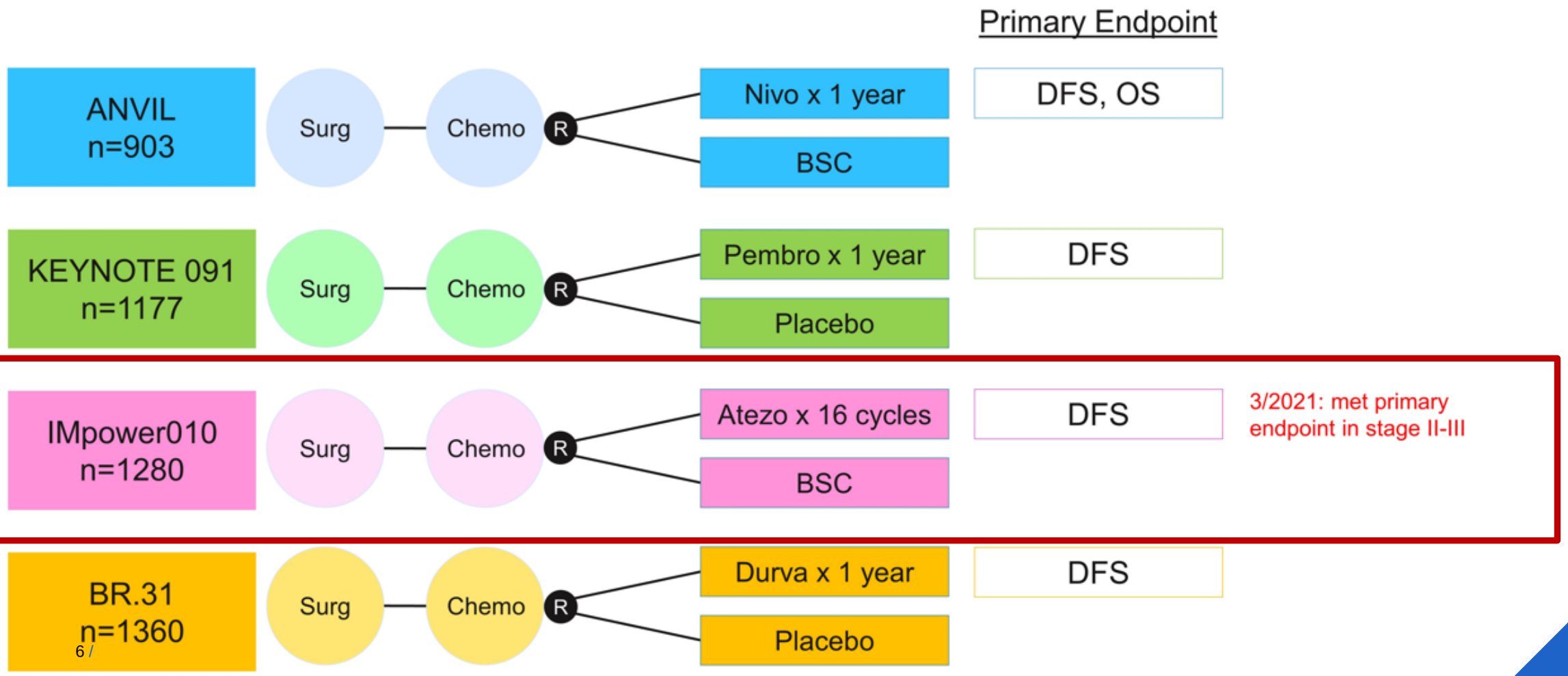
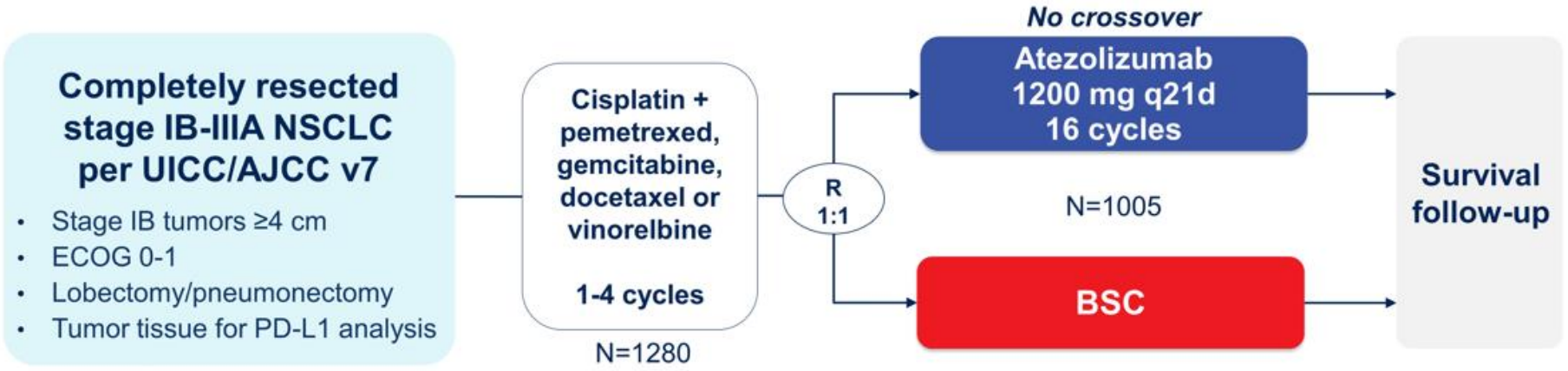
Phase III trials of adjuvant checkpoint inhibitors



Study design IMpower010

KEY POINTS:
- Overall a well designed and robust study
- AJCC 7th edition staging
- *All* randomized pts received adjuvant chemo
- SP263 assay used for efficacy analyses of PD-L1[1]
- 54.6% of patients had PDL1 ≥ 1%, slightly lower than in other studies (67% in PACIFIC[2])



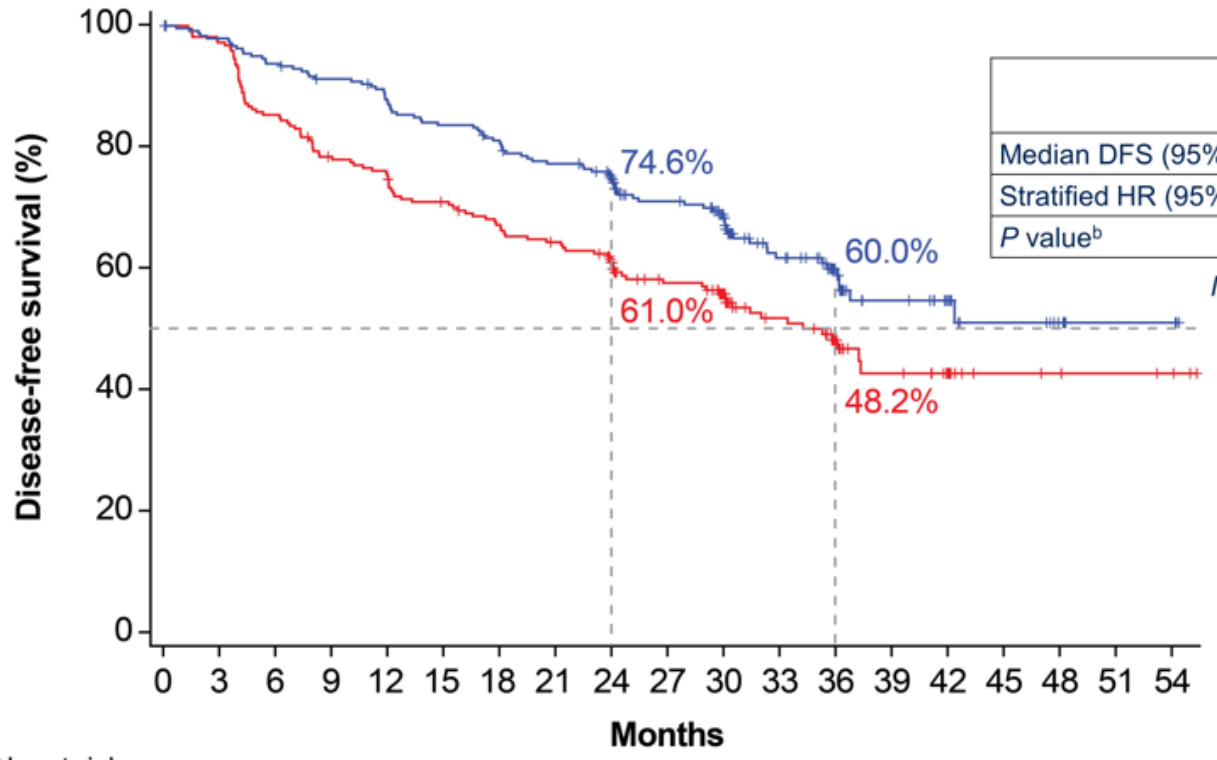
Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Abstract #8500

DFS in stage II-IIIA in PD-L1 TC ≥ 1 % (PE)



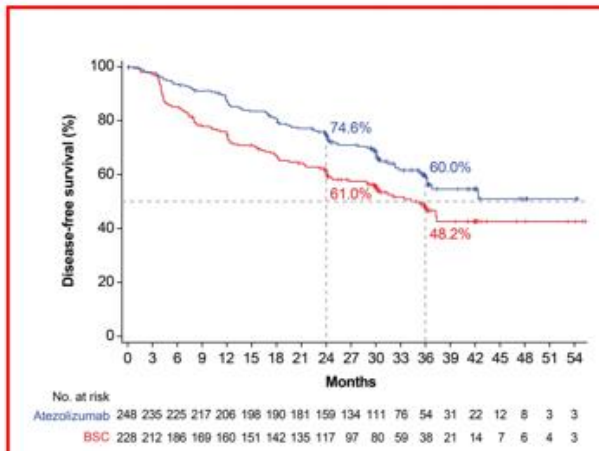
	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

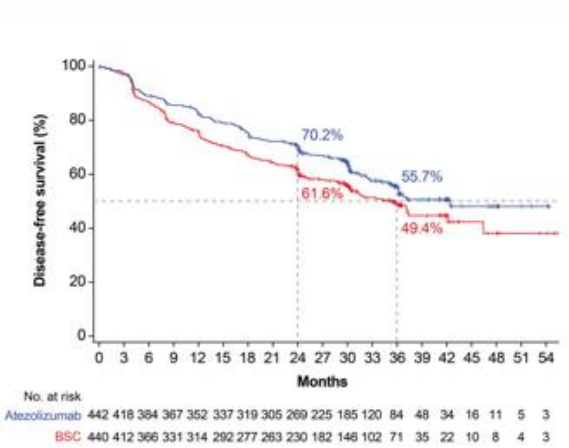
Median follow-up: 32.8 mo (range, 0.1-57.5)

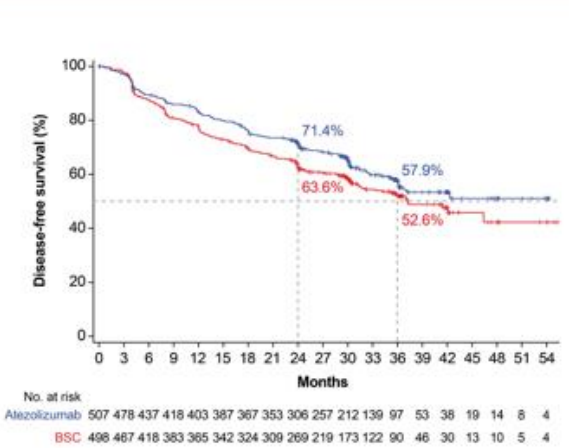
Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

Abstract #8500

Magnitude of benefit





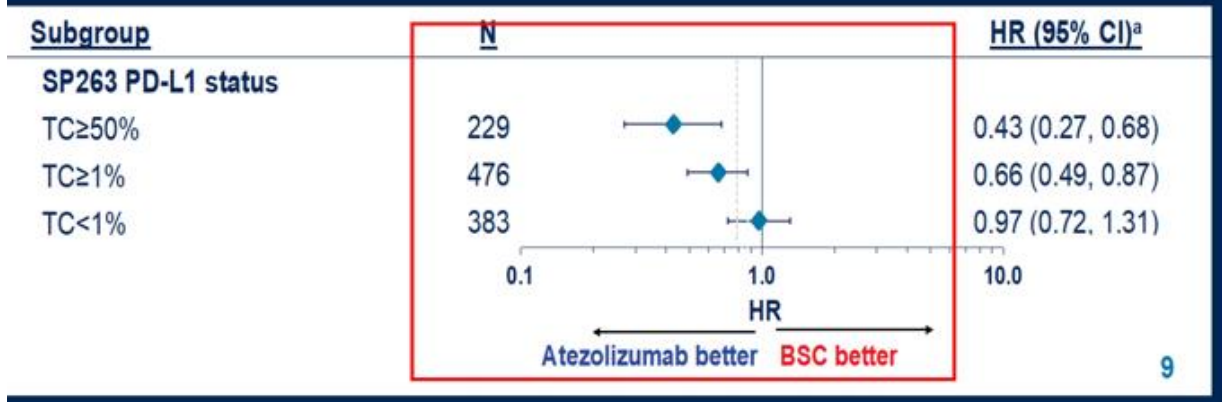


	PDL1 TC ≥ 1% , Stage II-IIIA	All randomized, Stage II-IIIA	ITT, stage IB-IIIA
DFS HR	0.66 (0.50, 0.88)	0.79 (0.64, 0.96)	0.81 (0.67, 0.99)
P Value	0.004	0.02	0.04

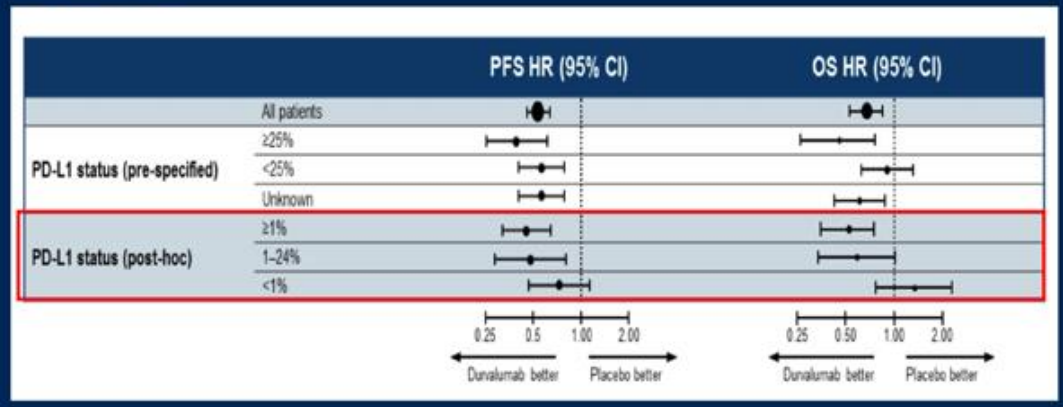
Abstract #8500

Biomarker selection

IMPower 010



PACIFIC[1]

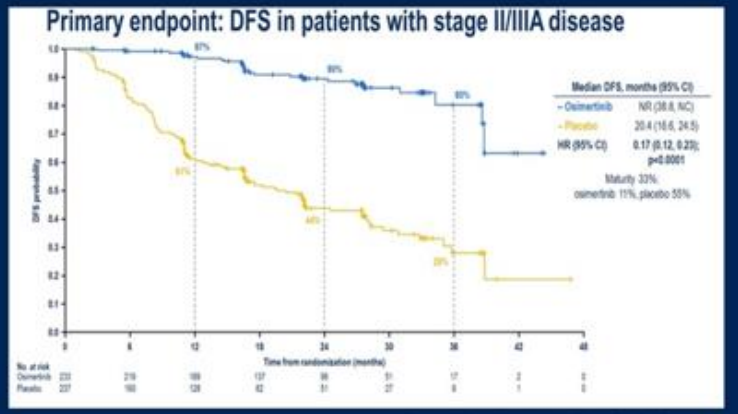


- As with other immunotherapy studies, the magnitude of benefit of adjuvant atezolizumab is greatest in patients with the highest levels of PD-L1.
- Among pts with PDL1 ≥ 50%, DFS HR 0.43
- Patients with negative PD-L1 did NOT benefit from adjuvant atezolizumab.

Atezolizumab: first IC with clinically meaningful benefit in adjuvant setting in PD-L1 positive stage II-IIIA NSCLC after chemo

Is DFS sufficient to change clinical practice?

- OS has historically been considered the “gold standard” for adjuvant studies, yet many ongoing studies are powered for DFS endpoints.
- OS data takes years to mature and, in the meantime, we (clinicians) have to make decisions based on available data.
- For patients and caregivers, improvements in disease free may translate into patient benefit, whether or not OS is improved.
- Recently, several adjuvant therapies (osimertinib, durvalumab) have received FDA approval based on DFS benefit, suggesting this is viewed as a clinically meaningful endpoint.

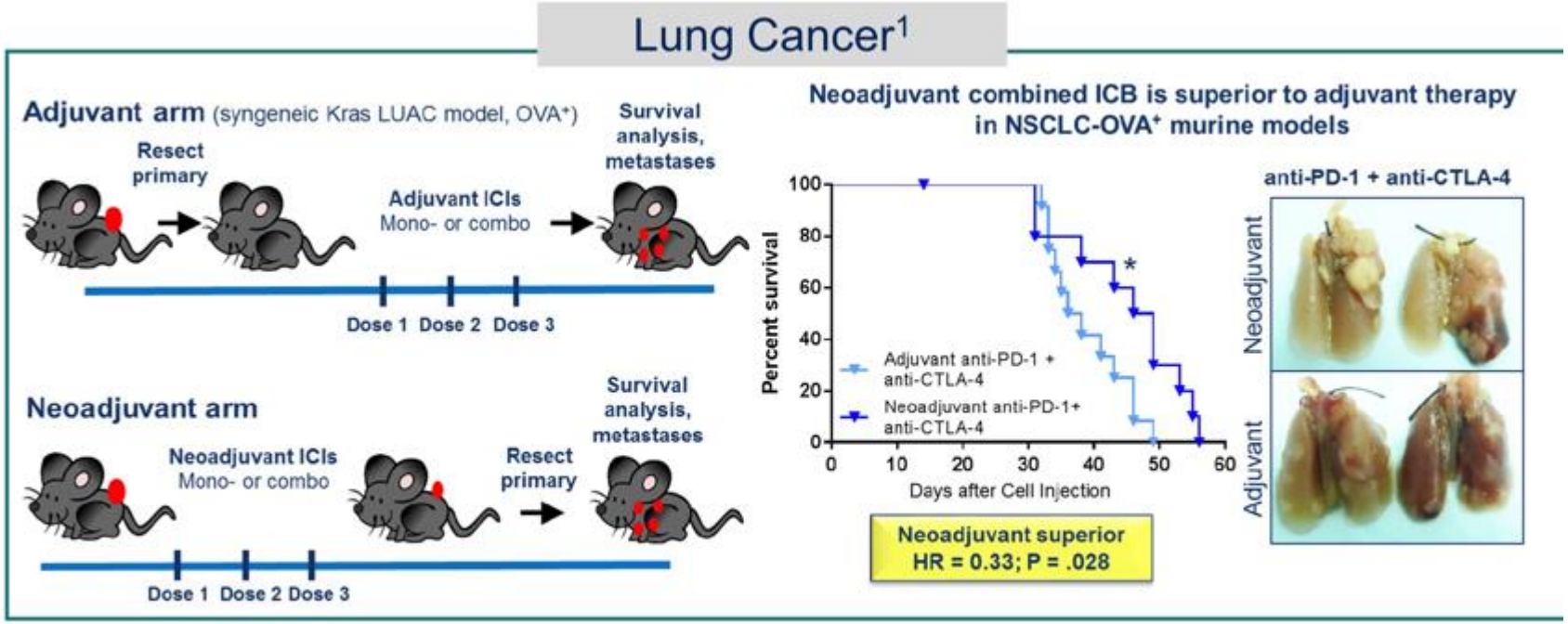


ADAURA (Herbst R, ASCO 2020)

Trial[1]	Drug	n	1º Endpoint	Estimated Completion Date	NCT
IMPower110	Atezolizumab	1005	DFS	December 2027	NCT02486718
ANVIL (EA5142)	Nivolumab	903	DFS + OS	January 2024	NCT02595944
KEYNOTE-091	Pembrolizumab	1177	DFS	February 2024	NCT02504372
BR.31	Durvalumab	1360	DFS	January 2024	NCT02273375

1. All data collected from clinicaltrials.gov, accessed 5/19/21

Rationale for neoadjuvant strategy

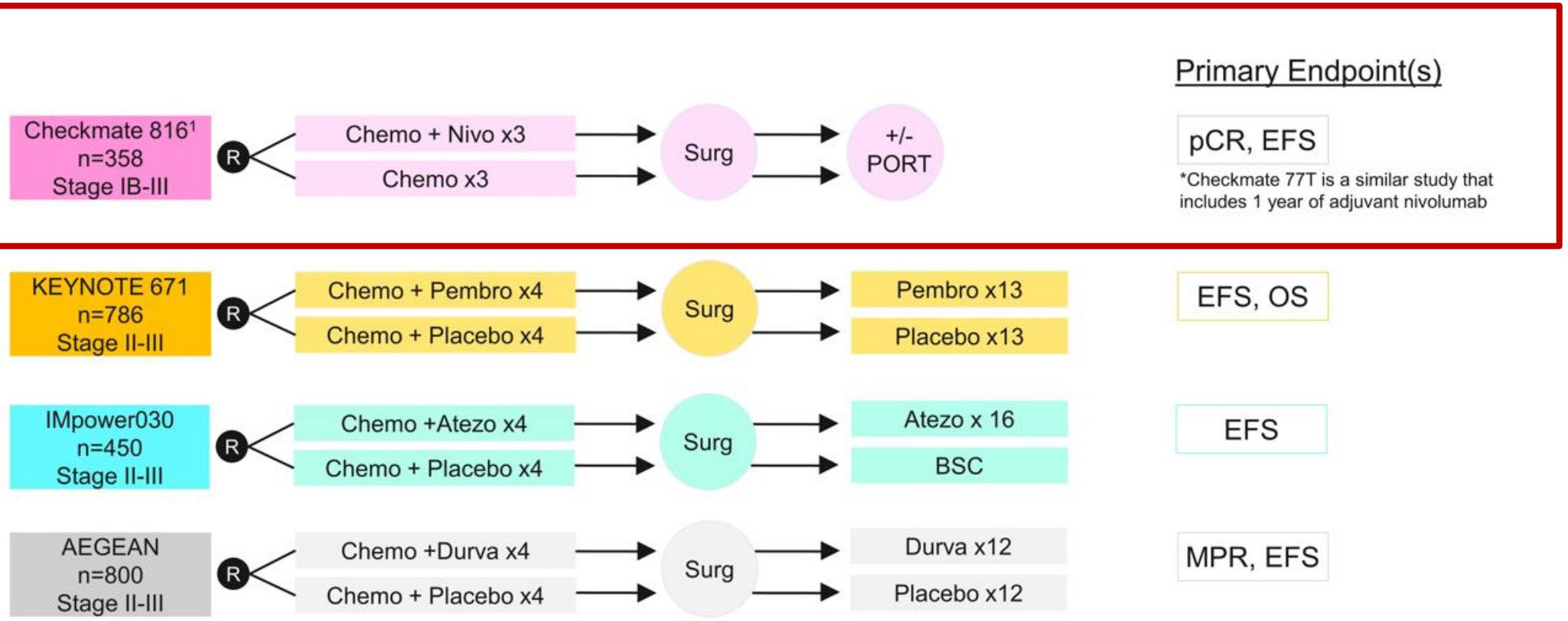


[1]Cascone ASCO 2019, [2]Liu Cancer Dis

Administering immunotherapy with the primary tumor intact = larger burden of endogenous tumor antigens, potentially:

(1) Enhancing tumor-specific T cell priming and trafficking
(2) Leading to more robust activation of the immune system
(3) Improving surveillance against micrometastatic disease

Phase III trials neoadjuvant chemo and PD(L)1 inhibitor



[1]Forde AACR 2021

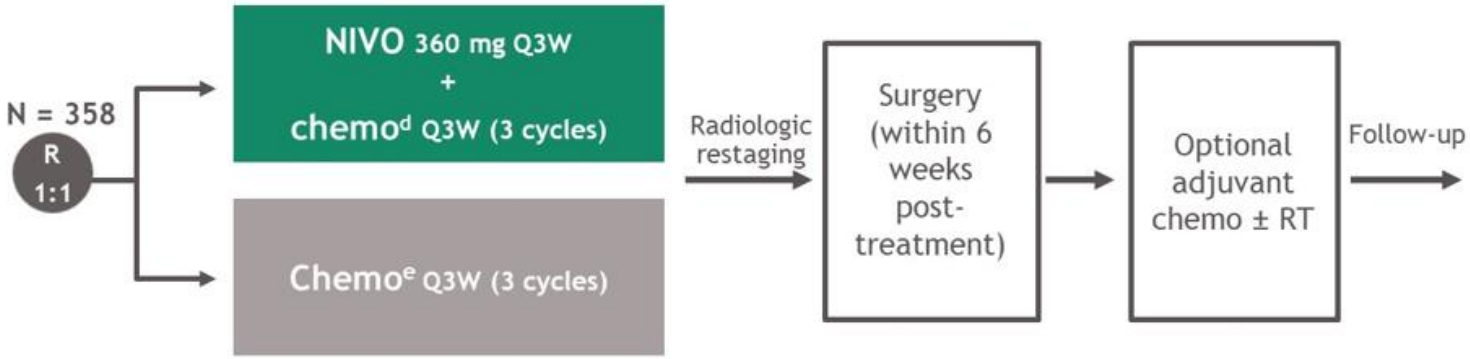
Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

Jonathan Spicer,[1] Changli Wang,[2] Fumihiro Tanaka,[3] Gene B. Saylors,[4] Ke-Neng Chen,[5] Moishe Liberman,[6] Everett Vokes,[7] Nicolas Girard,[8] Shun Lu,[9] Mariano Provencio,[10] Tetsuya Mitsudomi,[11] Mark M. Awad,[12] Enriqueta Felip,[13] Patrick M. Forde,[14] Scott J. Swanson,[12] Julie R. Brahmer,[14] Keith Kerr,[15] Cécile Dorange,[16] Junliang Cai,[16] Stephen Broderick[14]

Key eligibility criteria

- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
- ECOG PS 0-1
- No known sensitizing *EGFR* mutations or *ALK* alterations

Stratified by stage (IB/II vs IIIA), PD-L1[b] (≥ 1% vs < 1%[c]), and sex



Primary endpoints
- pCR by BIPR
- EFS by BICR

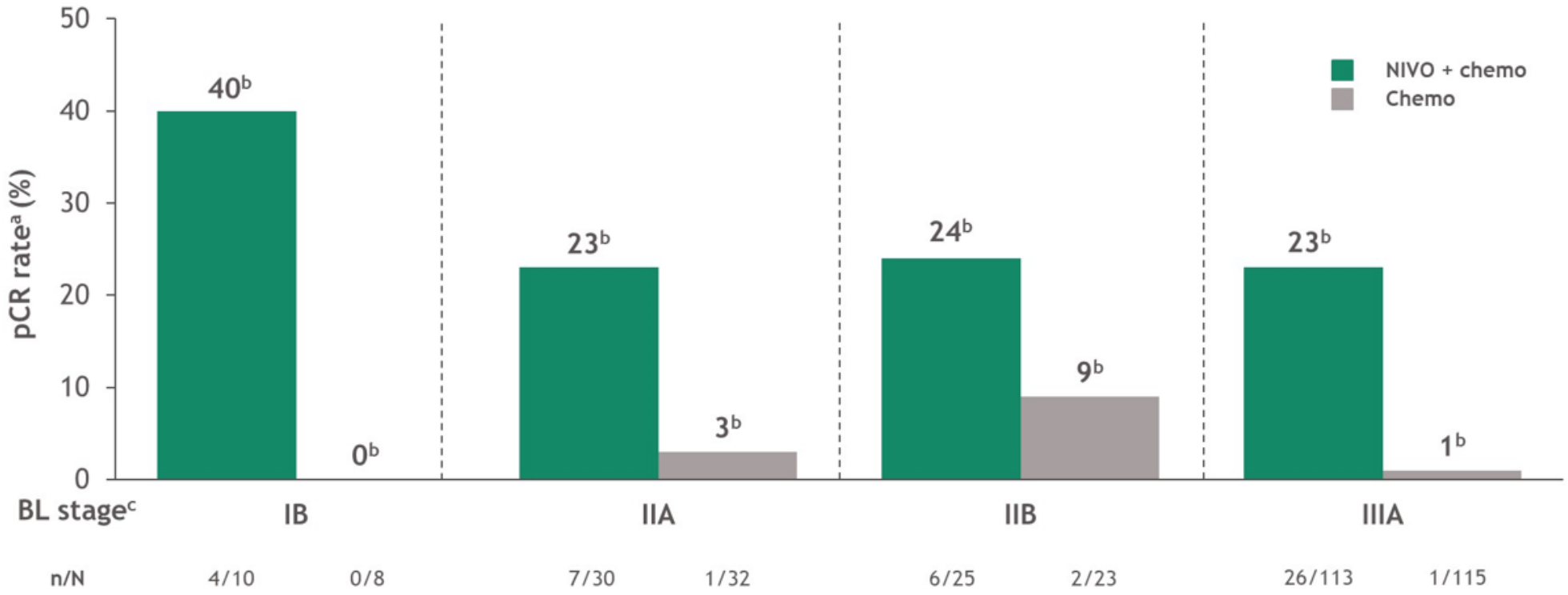
Key secondary endpoints
- MPR by BIPR
- OS
- Time to death or distant metastases

Key exploratory endpoints included
- ORR by BICR
- **Feasibility of surgery; peri- and post-operative surgery-related AEs**

Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

Abstract #8503

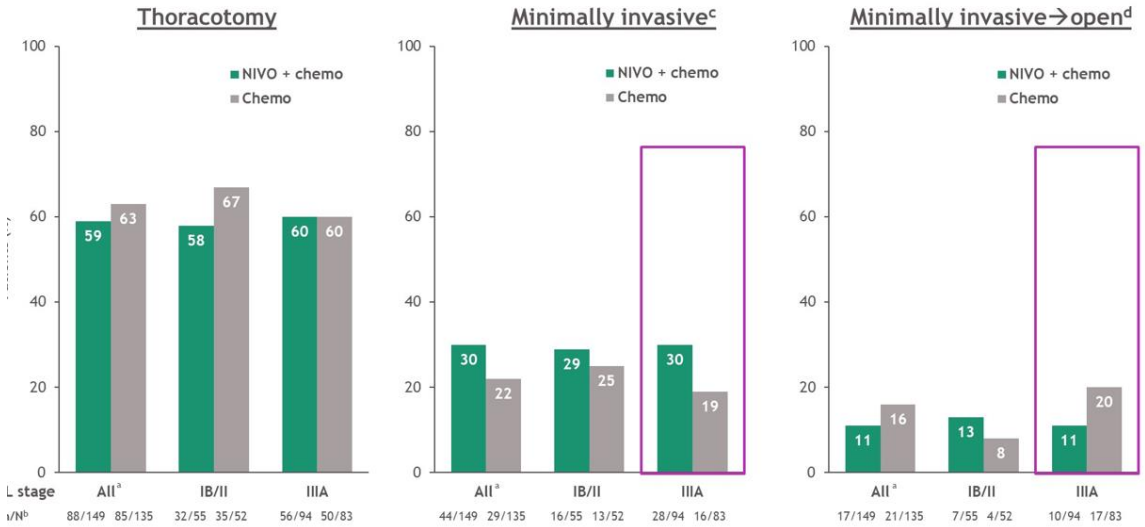
pCR by baseline disease stage

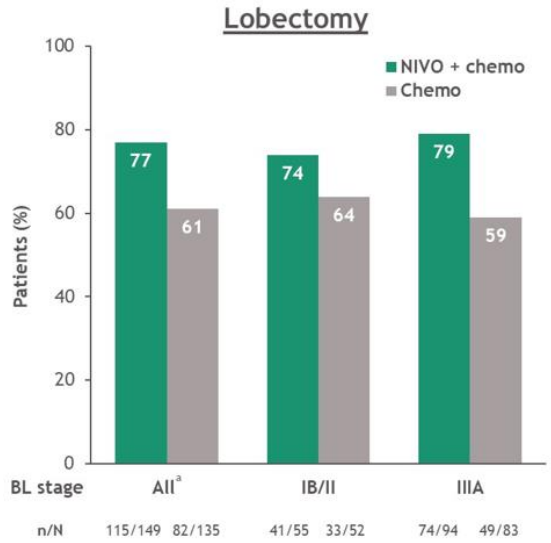


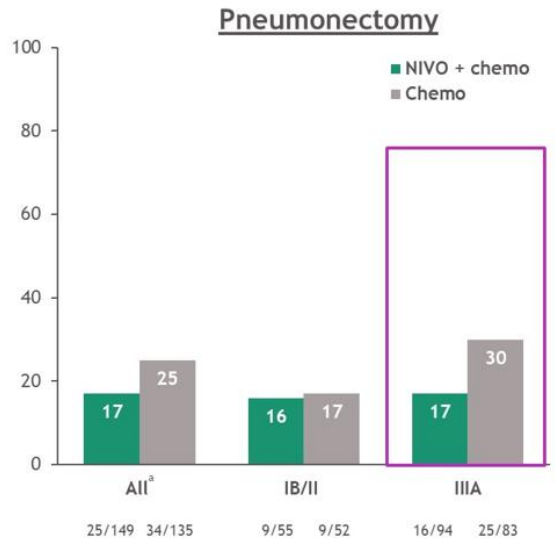
- pCR improvement with NIVO + chemo vs chemo was observed regardless of radiologic down-staging[d]

Abstract #8503

Surgical approach







In the chemoIO arm:

- More patients had the operation via a minimally invasive approach (VATS or robotic), including the patients with stage IIIA tumors at baseline
- Fewer patients required a pneumonectomy
- More patients had R0 resection

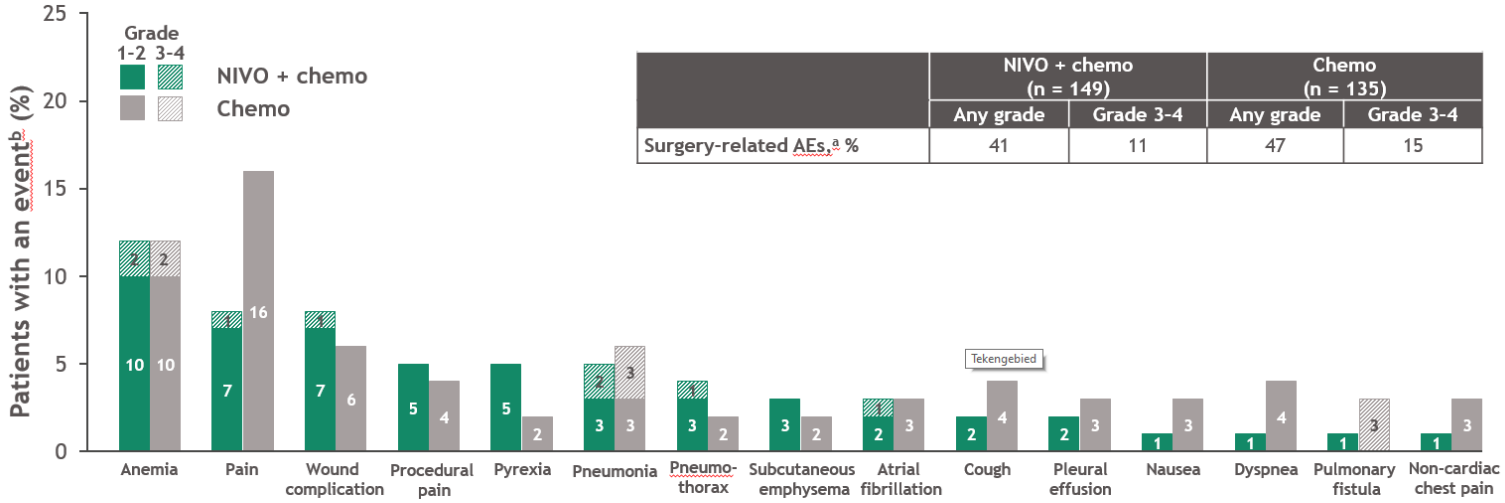
Abstract #8503

	All stages		Stage IB/II		Stage IIIA	
	NIVO + chemo (n = 149)	Chemo (n = 135)	NIVO + chemo (n = 55)	Chemo (n = 52)	NIVO + chemo (n = 94)	Chemo (n = 83)
Patients with delayed surgery,[b,c] n (%)	31 (21)	24 (18)	9 (16)	13 (25)	22 (23)	11 (13)
AE	6 (4)	9 (7)	2 (4)	7 (13)	4 (4)	2 (2)
Length of delay in surgery, weeks						
Median (IQR)	2.0 (0.6-3.0)	2.4 (1.0-3.7)	2.1 (0.9-2.9)	2.1 (1.3-3.6)	1.9 (0.6-3.0)	2.6 (0.6-4.9)
Of patients with delayed surgery, proportion n (%) with delay of[d]						
≤ 2 weeks	17 (55)	11 (46)	4 (44)	6 (46)	13 (59)	5 (46)
> 2 and ≤ 4 weeks	8 (26)	8 (33)	4 (44)	5 (38)	4 (18)	3 (27)
> 4 and ≤ 6 weeks	3 (10)	2 (8)	0	0	3 (14)	2 (18)
> 6 weeks	3 (10)	3 (12)	1 (11)	2 (15)	2 (9)	1 (9)

no delay in surgery

- Median (IQR) time from last neoadjuvant dose to definitive surgery was 5.3 (4.6-6.0) weeks with NIVO + chemo and 5.0 (4.6-5.9) weeks with chemo for all patients with definitive surgery

no increase in 90-day surgical toxicity



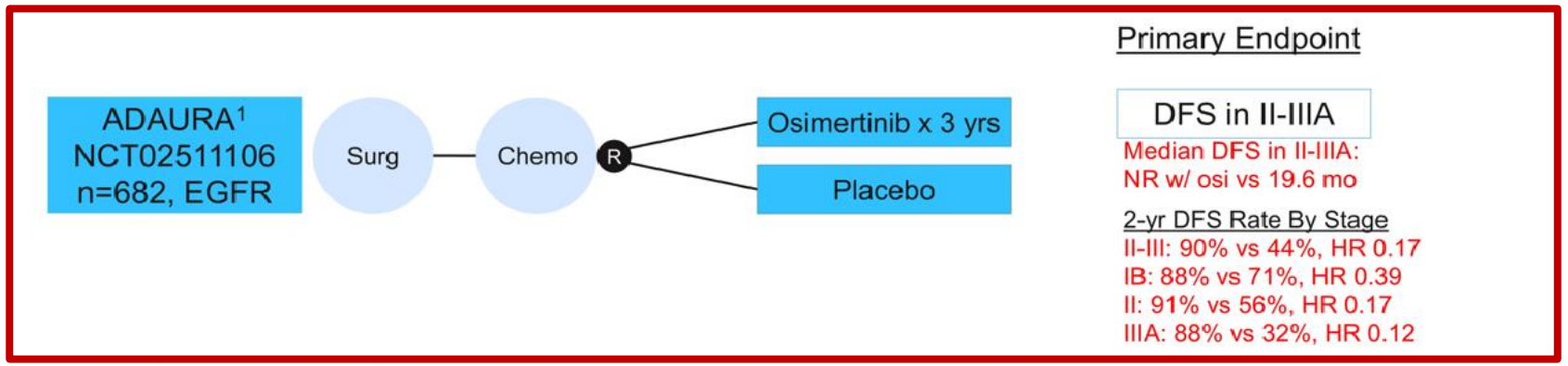
	NIVO + chemo (n = 149)		Chemo (n = 135)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Surgery-related AEs,[a] %	41	11	47	15

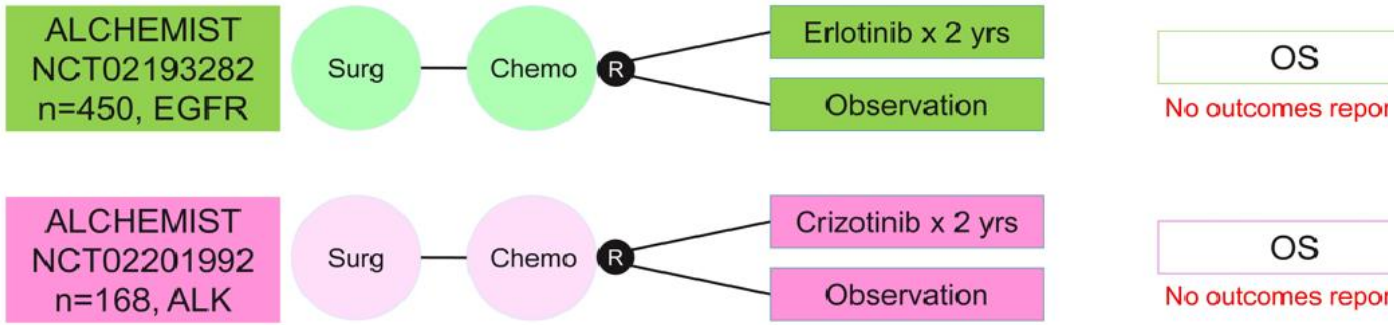
- Grade 5 surgery-related AEs (within 24 hours of AE onset) were reported in 2 patients in the NIVO + chemo arm and were deemed unrelated to study drug per investigator (1 each due to pulmonary embolism and aortic rupture)[c]
- 30-day and 90-day mortality rates are planned to be evaluated when survival endpoints are available

- no delay in surgery
- no impairment of surgery
- no reduction in completeness of resection
- no increase in 90-day surgical toxicity
- more event-free and OS data are needed for CM816 to become practice changing

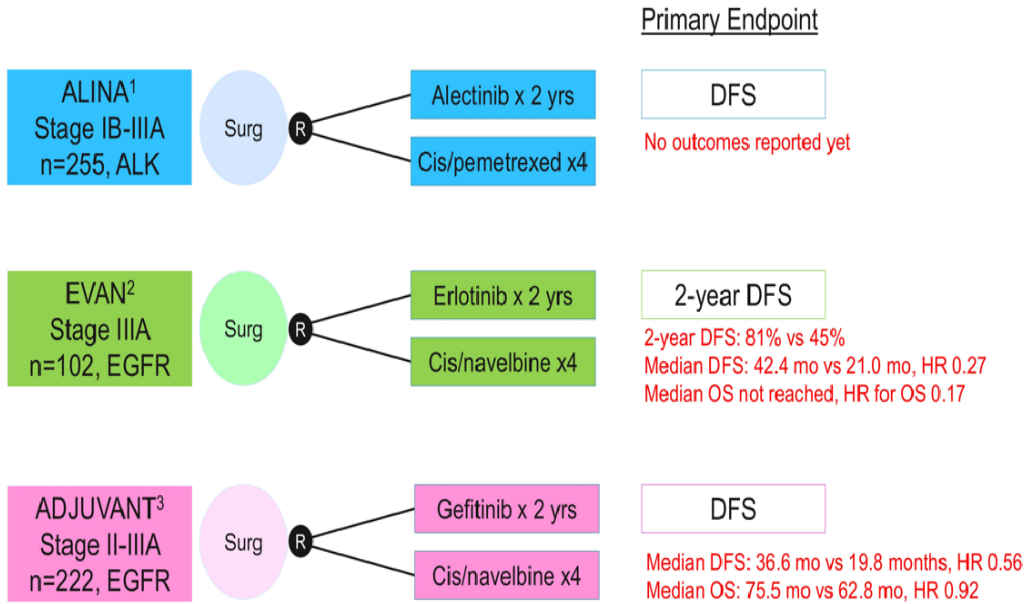
Phase III trials adjuvant targeted therapy

ASCO 2020





EJM 2020



[1]03456076, [2]Yue Lancet Respir Med 2018, [3]ADJUVANT-CTONG1104 Zhong JCO 2021

Adjuvant gefitinib versus cisplatin/vinorelbine in Japanese patients with completely resected, EGFR-mutated, stage II–III non-small-cell lung cancer (IMPACT: WJOG6410L): a randomized phase 3 trial.

Hirohito Tada,[1] Tetsuya Mitsudomi,[2] Takeharu Yamanaka,[3] Kenji Sugio,[4] Masahiro Tsuboi,[5] Isamu Okamoto,[6] Yasuo Iwamoto,[7] Noriaki Sakakura,[8] Shunichi Sugawara,[9] Shinji Atagi,[10] Toshiaki Takahashi,[11] Hidetoshi Hayashi,[2] Morihito Okada,[12] Hidetoshi Inogawa,[13] Hiroshige Yoshioka,[14] Kazuhisa Takahashi,[15] Masahiko Higashiyama,[16] Ichiro Yoshino,[17] Kazuhiko Nakagawa,[2] West Japan Oncology Group

Phase 3 RCT (IMPACT)

Study design

Completely resected stage II-III NSCLC
Lobectomy or more
EGFR mutation (Ex19-del or L858R)
Without T790M
ECOG PS 0-1 Age ≧20 & <75 years
N=230

→ R

Gefitinib 250mg/day for 24 months
or until disease progression
or unacceptable toxicity

Cisplatin 80mg/m2 day1
plus vinorelbine 25mg/m2 day1 and 8
every 3 weeks, for 4 cycles

Stratification factors
- institute
- stage II vs. III
  - UICC TNM classification (7th version)
- gender
- age <65 or ≧65

Efficacy assessment schedules
every 6 months :
- contrast chest/abdominal CT

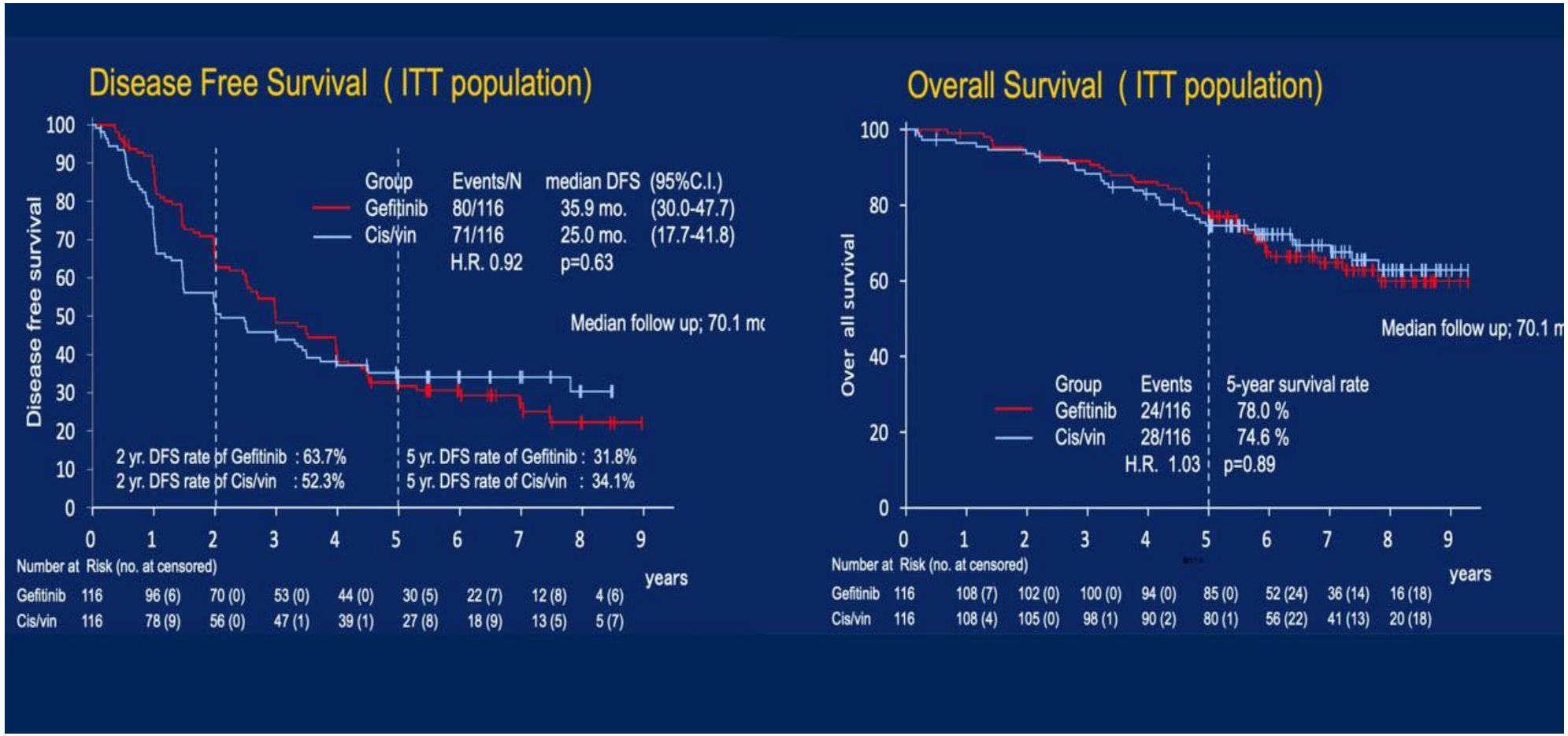
every 12 moths : brain MRI. PET/CT or bone scan

Primary endpoint :
- Disease free survival by BICRC.

Secondary endpoint
- Overall survival
- Safety and tolerability
- Relapse pattern

UMIN000006252

Abstract #8501



DFS: numerically longer with gefitinib, but HR 0.92
OS: not significantly different, HR 1.03

Abstract #8501

Phase 2 RCT (CTONG1103)

- **Study objective**
  - To evaluate the long-term efficacy and safety of neoadjuvant erlotinib in patients with stage IIIA-N2 EGFR-mutant NSCLC in CTONG1103

Key patient inclusion criteria
- Stage IIIA-N2 NSCLC
- EGFR mutation (exon 19 or exon 21)
- Treatment naïve
- ECOG PS 0–1

(n=72)

R 1:1

Neoadjuvant

Erlotinib 150 mg/day for 42 days (n=37)

Stratification
- LN status, histology, smoking status, gender

Cisplatin 75 mg/m^2 + gemcitabine 1250 mg/m^2 q3w for 2 cycles (n=35)

Non-PD

SURGERY

Adjuvant

Erlotinib 150 mg/day for up to 12 months

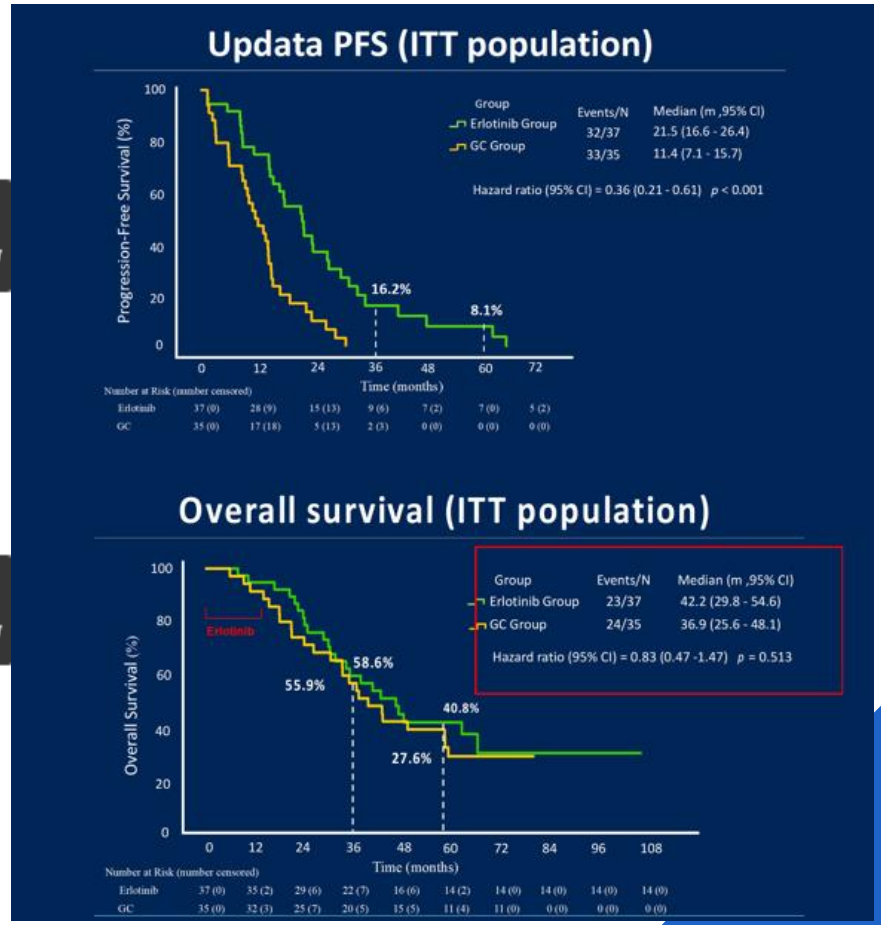
Cisplatin 75 mg/m^2 D1 + gemcitabine 1250 mg/m^2 D1, 8 q3w for 2 cycles

PD/ toxicity

PD/ toxicity

Primary endpoint
- ORR (RECIST v1.1)

Secondary endpoints
- pCR, downstaging, PFS, OS, safety



Abstract #8502

- 3 RCT on (neo)adjuvant EGFR-TKI with mature OS data
- TKI for up to 2 years compared to 4 cycles of cis-based chemo
- initial DFS advantage, no OS benefit
- follow-up results of osimertinib in ADAURA are needed

Local treatment modalities

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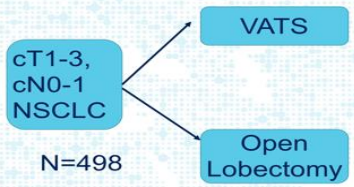
2021 ASCO ANNUAL MEETING

VIDEO-ASSISTED THORACOSCOPIC VERSUS OPEN LOBECTOMY IN PATIENTS WITH EARLY-STAGE LUNG CANCER: ONE-YEAR RESULTS FROM A RANDOMIZED CONTROLLED TRIAL (VIOLET)

Eric Lim, Tim JP Batchelor, Joel Dunning, Michael Shackcloth, Vladimir Anikin, Babu Naidu, Elizabeth Belcher, Mahmoud Loubani, Vipin Zamvar, Rosie A Harris, Lucy Dabner, Holly E McKeon, Sangeetha Paramasivan, Alba Realpe, Daisy Elliott, Paulo De Sousa, Jane Blazeby, Chris A Rogers on behalf of The VIOLET Trialists

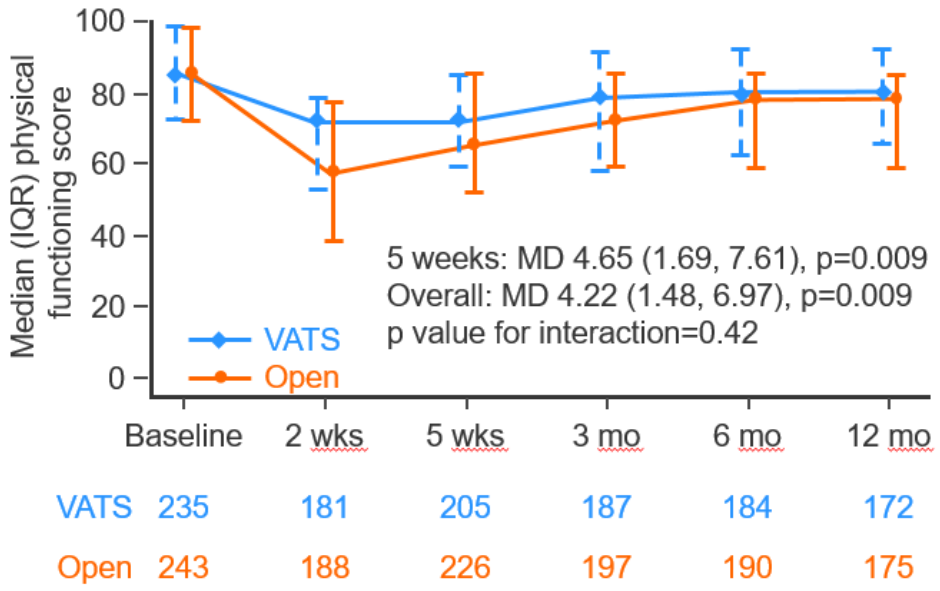
Primary Outcome:
Physical Function at 5 weeks



Violet STUDY | BRISTOL TRIALS CENTRE | Royal Brompton & Harefield NHS Foundation Trust | Imperial College London

VIOLET (QoL)

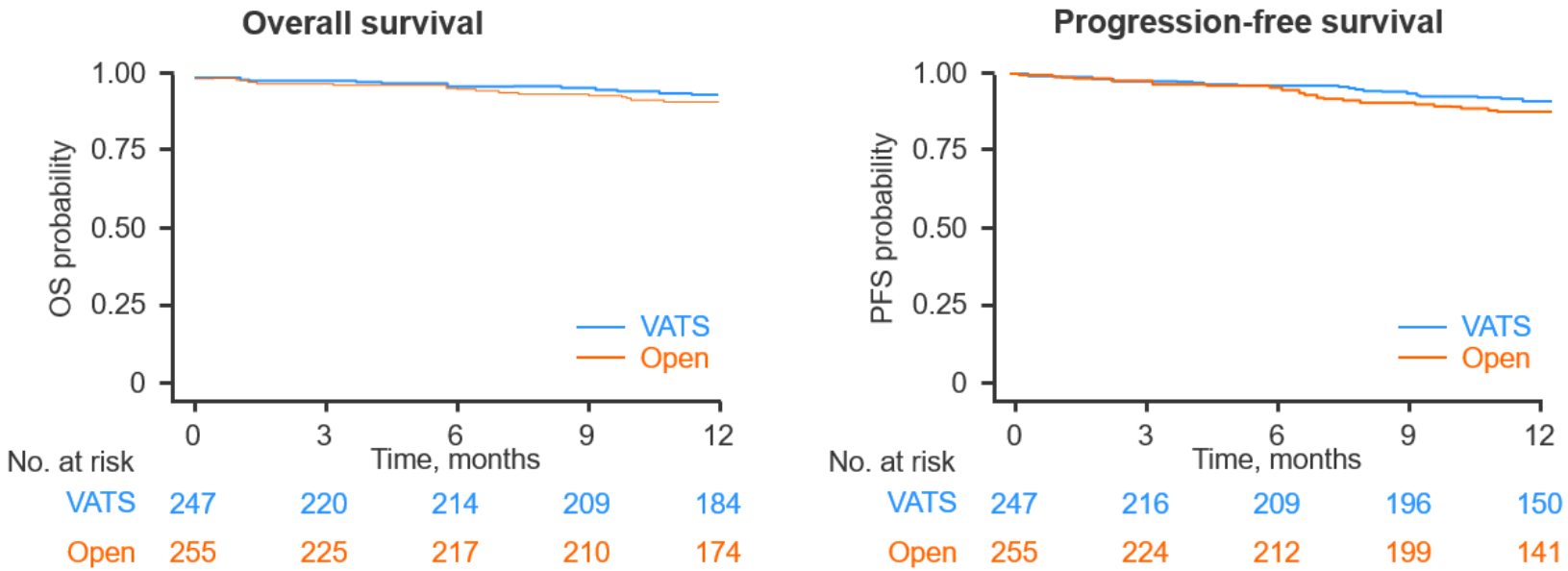
Physical function at 1 year



Outcome, MD (95%CI); p-value	Primary analysis	Analysis excluding benign patients
QLQ-C30 physical function at 5 weeks	4.65 (1.69, 761); 0.0089	4.66 (1.71, 7,62); 0.0089
In-hospital pain	−0.02 (−0.46, 0.41)	−0.54 (−0.99, −0.09)

Outcome	VATS (n=247)	Open surgery (n=255)	RR (95%CI); p-value
In-hospital before discharge, n (%)			
Any AE	81 (32.8)	113 (44.3)	0.74 (0.66, 0.84); <0.001
Any SAE	20 (8.1)	21 (8.2)	0.98 (0.59, 1.63); 0.948
After discharge following surgery, events/patients (%)			
Readmissions	117/70 (29.0)	141/88 (35.9)	
SAE	142/75 (30.7)	207/94 (37.8)	0.81 (0.66, 1.00); 0.053

VIOLET (oncological outcomes)



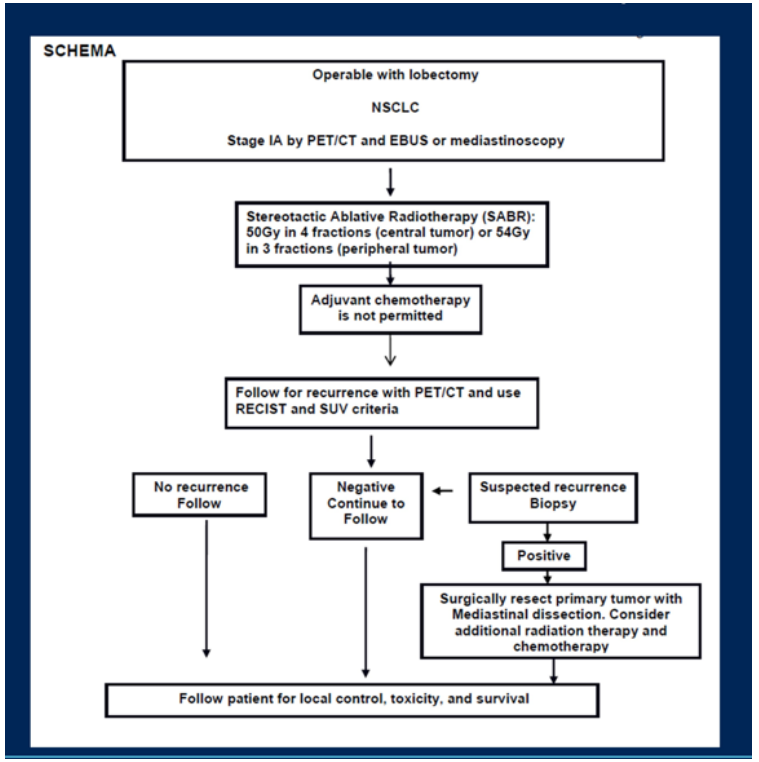
Outcome, HR (95%CI); p-value	Primary analysis	Analysis adjusting for pathological disease stage
OS	0.67 (0.32, 1.40); 0.283	0.71 (0.34, 1.50); 0.366
PFS	0.73 (0.42, 1.27); 0.262	0.75 (0.42, 1.32); 0.312

reinforce the paradigm shift in surgical approach
improved results without compromising oncological outcomes

2021 ASCO ANNUAL MEETING

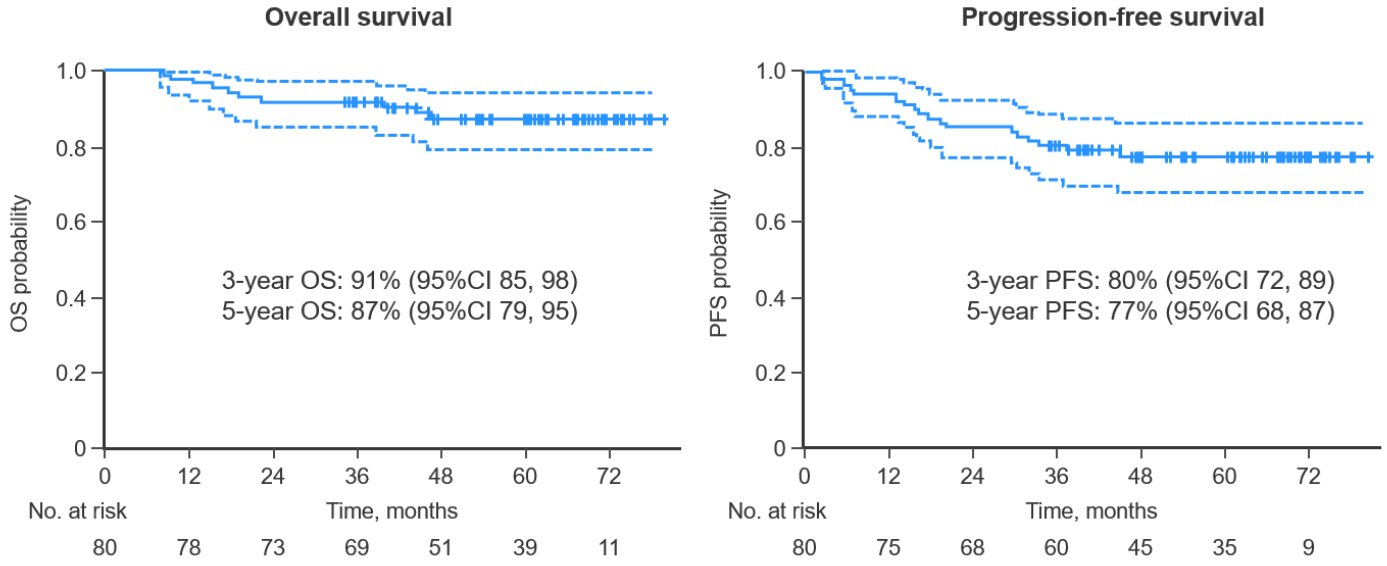
STEREOTACTIC ABLATIVE RADIOTHERAPY IN OPERABLE STAGE I NSCLC PATIENTS: LONG-TERM RESULTS OF THE EXPANDED STARS CLINICAL TRIAL

Joe Y. Chang, Reza J Mehran, Lei Feng, Stephen McRae,
Peter Balter, Donald Berry and Jack A Roth
On behalf of The STARS Lung Cancer Clinical Trials Group

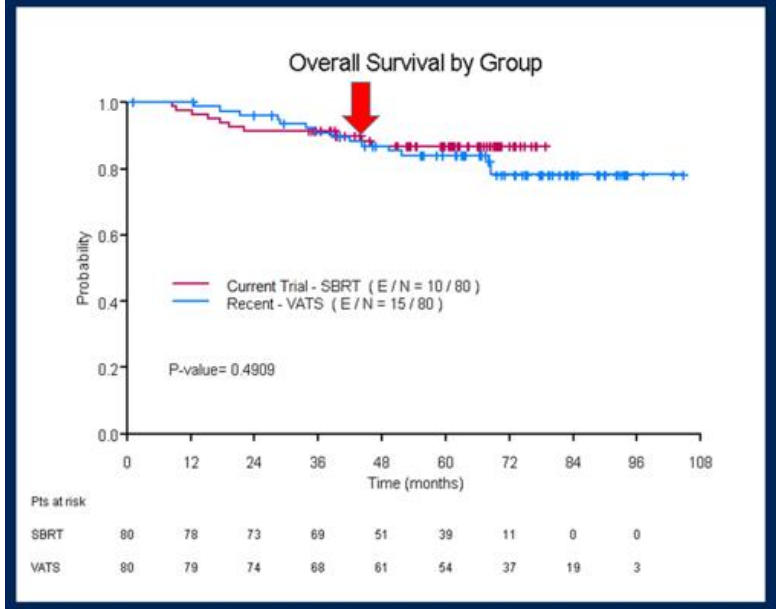


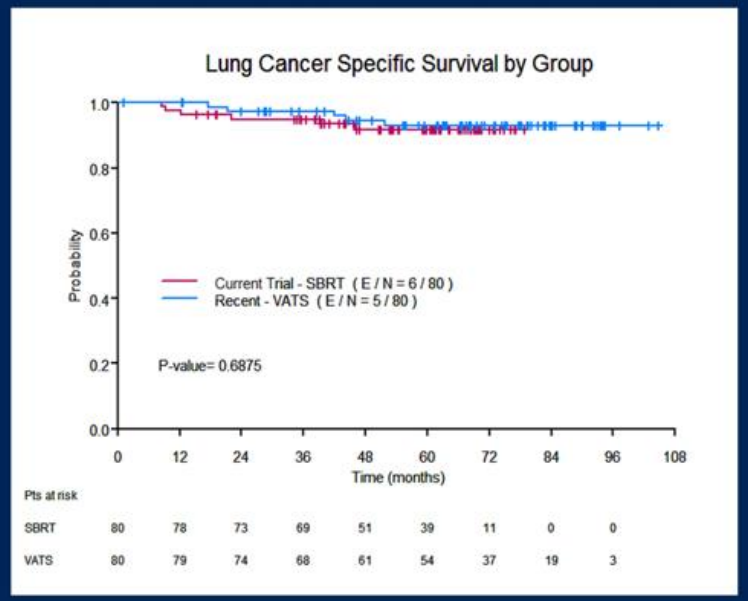
Expanded single-arm trial in operable stage IA risk-factor matched comparison with historical VATS data (n=229)

PE: OS at 3 years

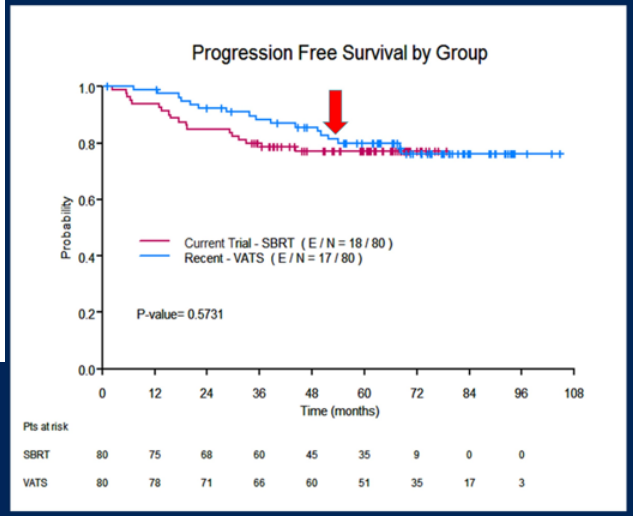


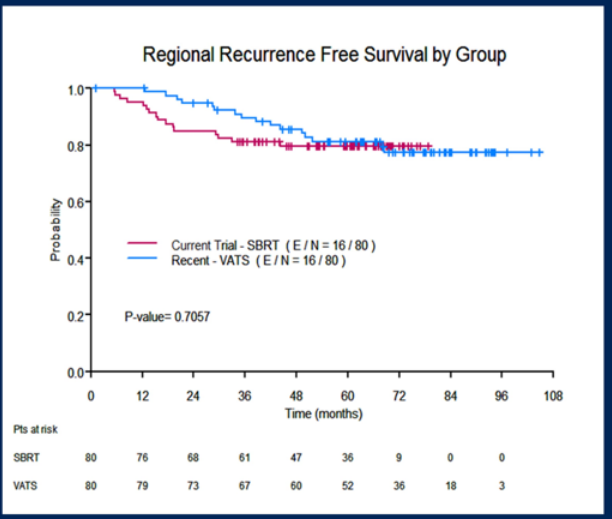
OS/PFS data SABR and VATS





OS: 3-Y: 91% vs 91%
5-Y: 87% vs 84%
HR: 0.78 (95% CI: 0.35~1.76; p=0.55)
Non- inferiority is claimed





PFS: 3-Y: 80% vs 88%
5-Y: 77% vs 80%
HR: 1.29 (95% CI 0.66-2.53, p= 0.46)

Unresectable stage III

Update PACIFIC

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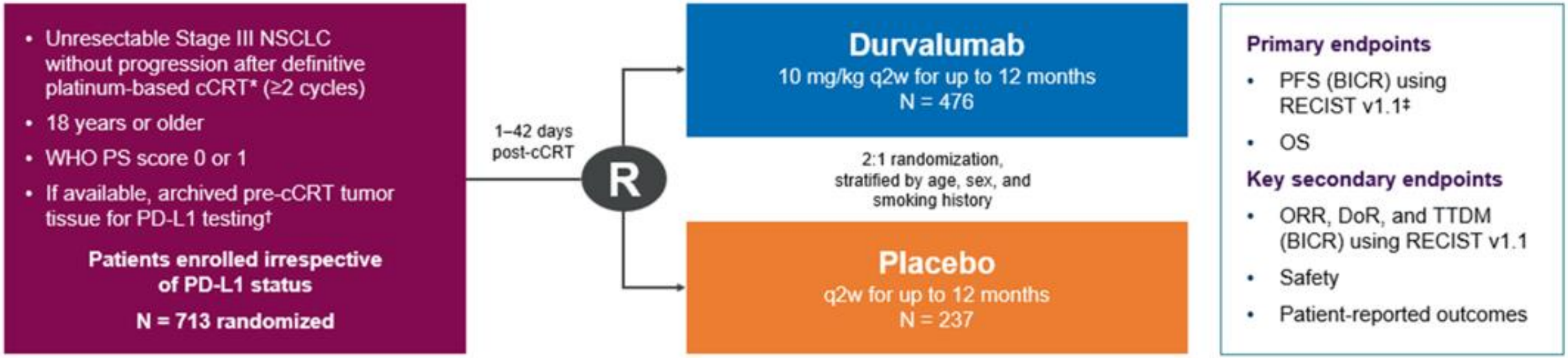
PACIFIC (5-year mature OS analysis)



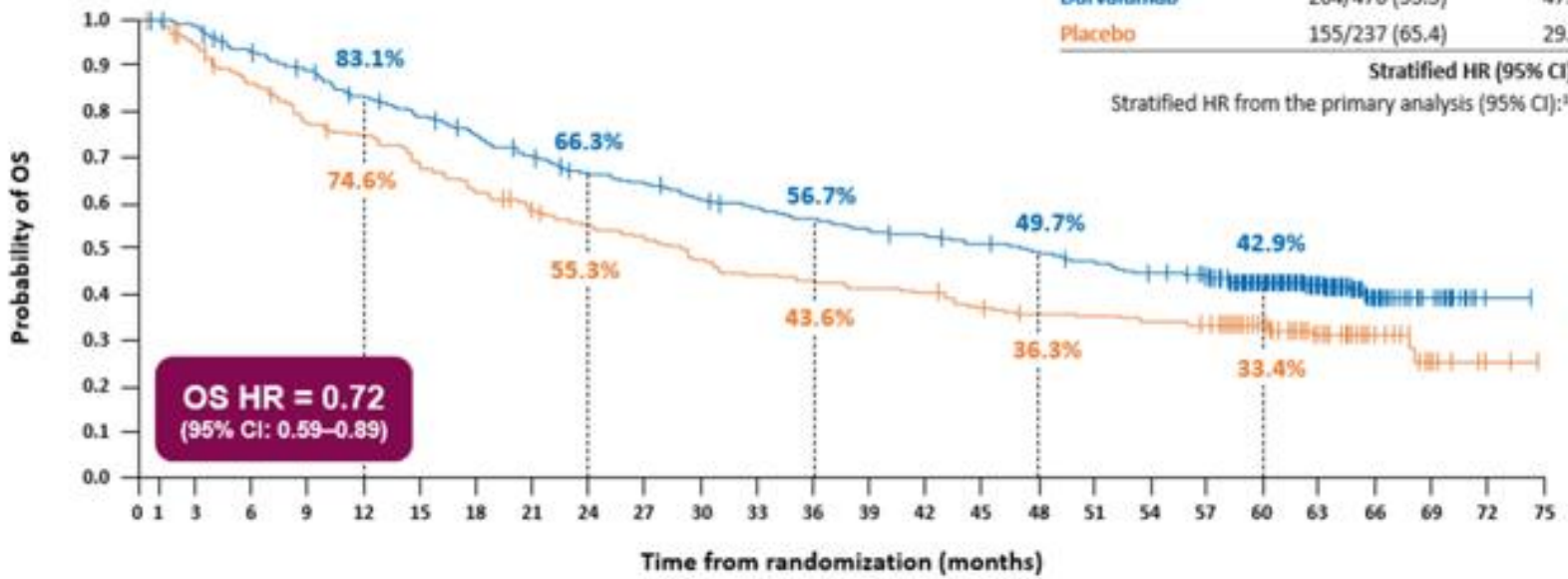
- **Updated analyses of OS and PFS, assessed ~5 years after the last patient was randomized (data cutoff: 11 January 2021; exploratory, post-hoc analysis)**

Abstract #8511

	No. of events/ total no. of patients (%)	Median OS (95% CI), months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)

Stratified HR (95% CI): 0.72 (0.59–0.89)

Stratified HR from the primary analysis (95% CI):[1,2] 0.68 (0.53–0.87)



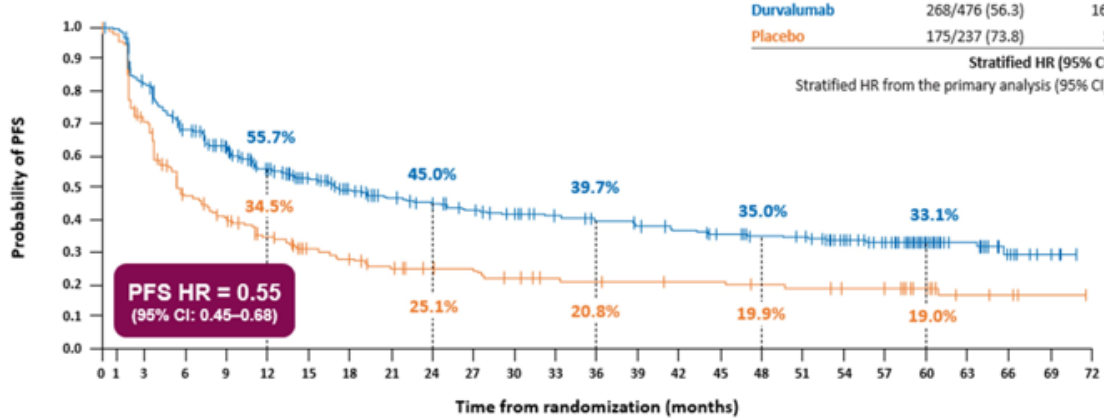
No. at risk

Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

	No. of events/ total no. of patients (%)	Median PFS (95% CI), months
Durvalumab	268/476 (56.3)	16.9 (13.0–23.9)
Placebo	175/237 (73.8)	5.6 (4.8–7.7)

Stratified HR (95% CI): 0.55 (0.45–0.68)

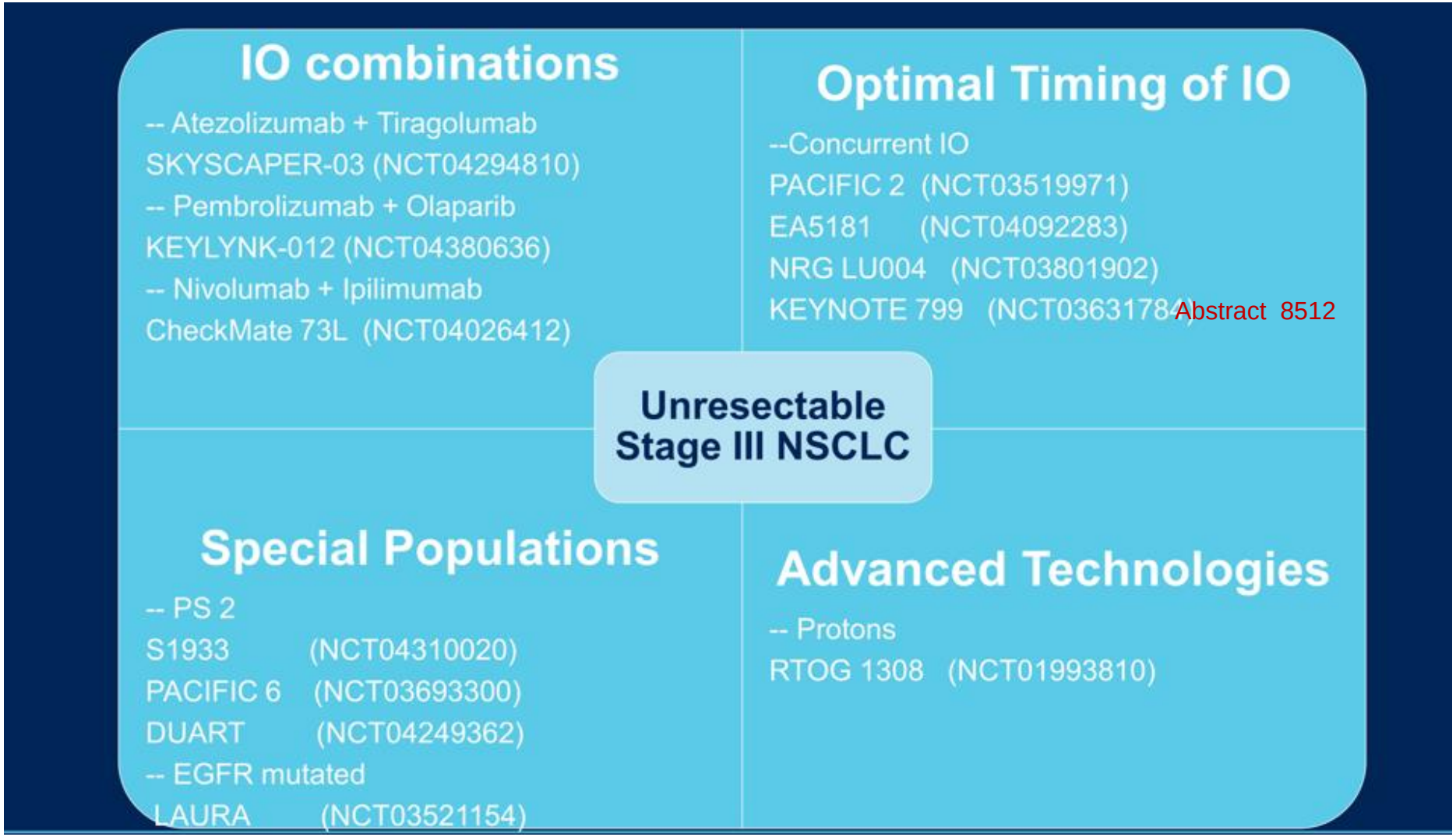
Stratified HR from the primary analysis (95% CI):[1] 0.52 (0.42–0.65)



No. at risk

Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

Unresectable stage III: clinical trial landscape



Metastatic NSCLC non-oncogene addicted

CheckMate-9LA
CheckMate-227

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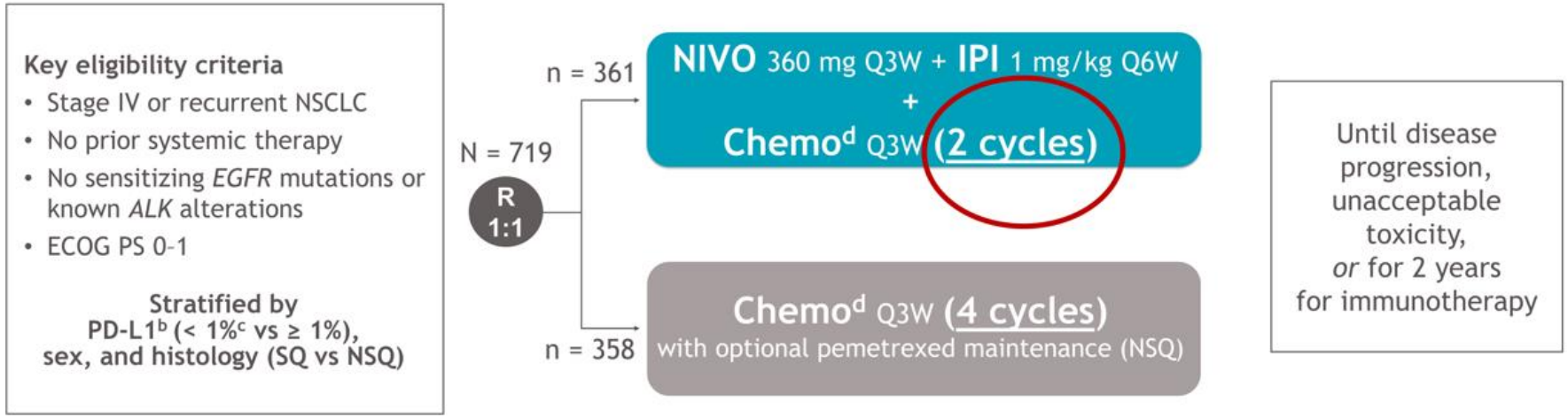
CheckMate 9LA

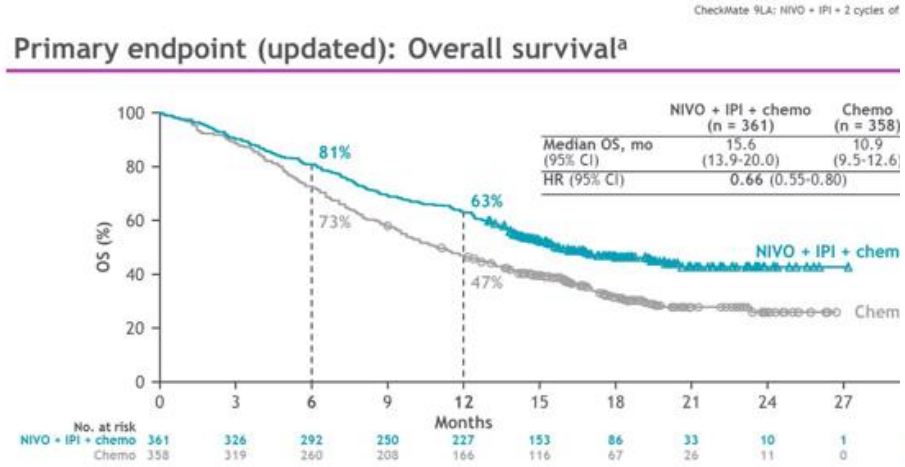


DBL: February 18, 2021; minimum / median follow-up for OS: 24.4 months / 30.7 months.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

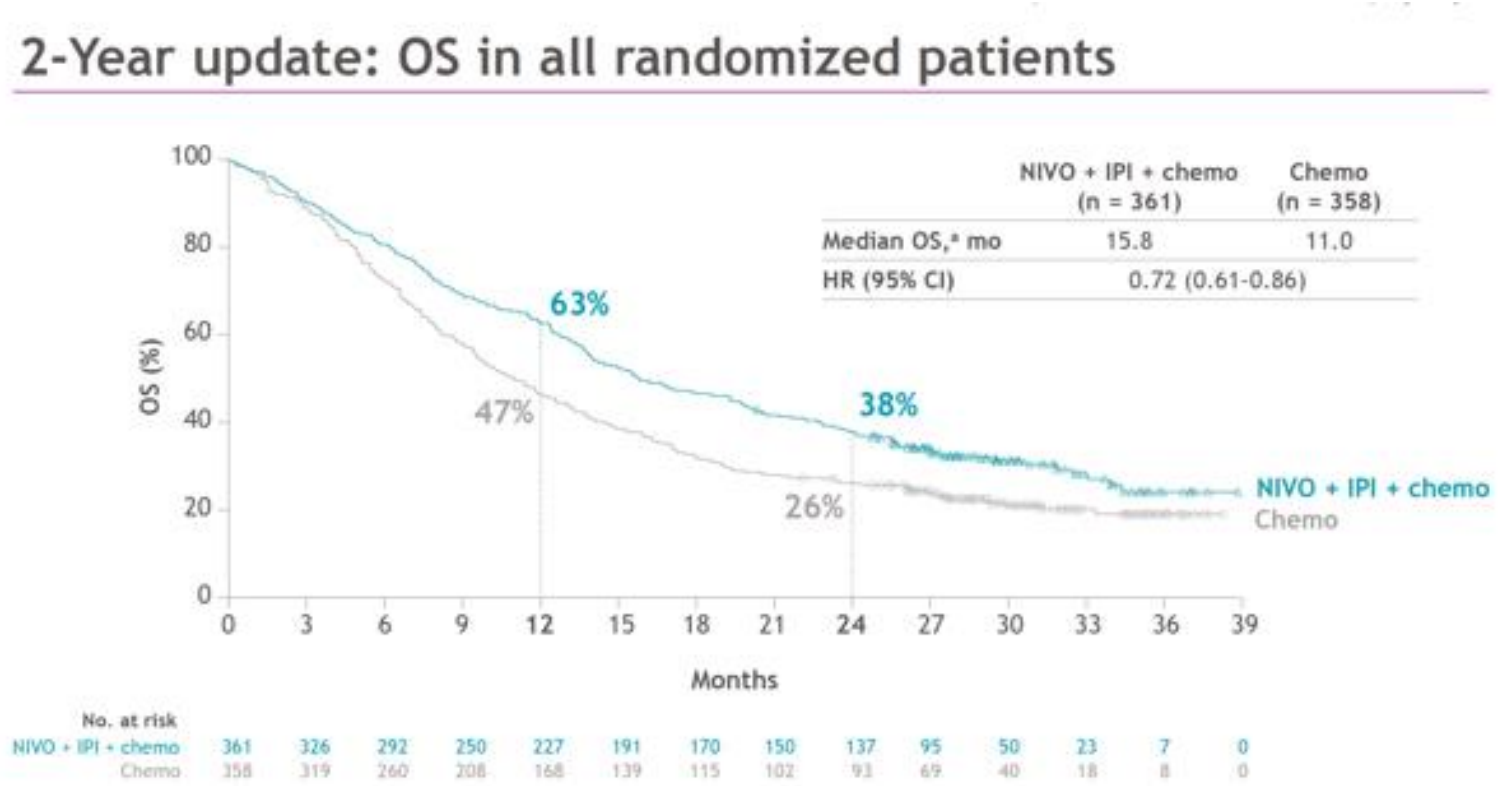
Abstract #9000

Additional follow-up



Minimum follow-up 12.7 months

ASCO 2020



ASCO 2021

Subgroup	Median OS, mo NIVO + IPI + chemo n = 361	Median OS, mo Chemo n = 358	Unstratified HR
All randomized (N = 719)	15.8	11.0	0.73
< 65 years (n = 354)	15.9	10.7	0.64
≥ 65 to < 75 years (n = 295)	19.0	11.9	0.78
≥ 75 years (n = 70)	8.5	11.5	1.04
Male (n = 504)	14.2	9.8	0.72
Female (n = 215)	22.2	15.9	0.75
ECOG PS 0 (n = 225)	27.1	14.1	0.54
ECOG PS 1 (n = 492)	13.6	9.7	0.83
Never smoker (n = 98)	14.1	14.4	1.08
Smoker (n = 621)	16.2	10.4	0.68
SQ (n = 227)	14.5	9.1	0.63
NSQ (n = 492)	17.8	12.0	0.78
Liver metastases (n = 154)	10.2	8.1	0.85
No liver metastases (n = 565)	19.3	12.4	0.72
Bone metastases (n = 207)	11.9	8.3	0.73
No bone metastases (n = 512)	19.7	12.4	0.74
CNS metastases (n = 123)	19.9	7.9	0.47
No CNS metastases (n = 596)	15.6	11.8	0.79
PD-L1 < 1% (n = 264)	17.7	9.8	0.67
PD-L1 ≥ 1% (n = 407)	15.8	10.9	0.70
PD-L1 1-49% (n = 233)	15.2	10.4	0.70
PD-L1 ≥ 50% (n = 174)	18.9	12.9	0.67

Unstratified HR (95% CI)

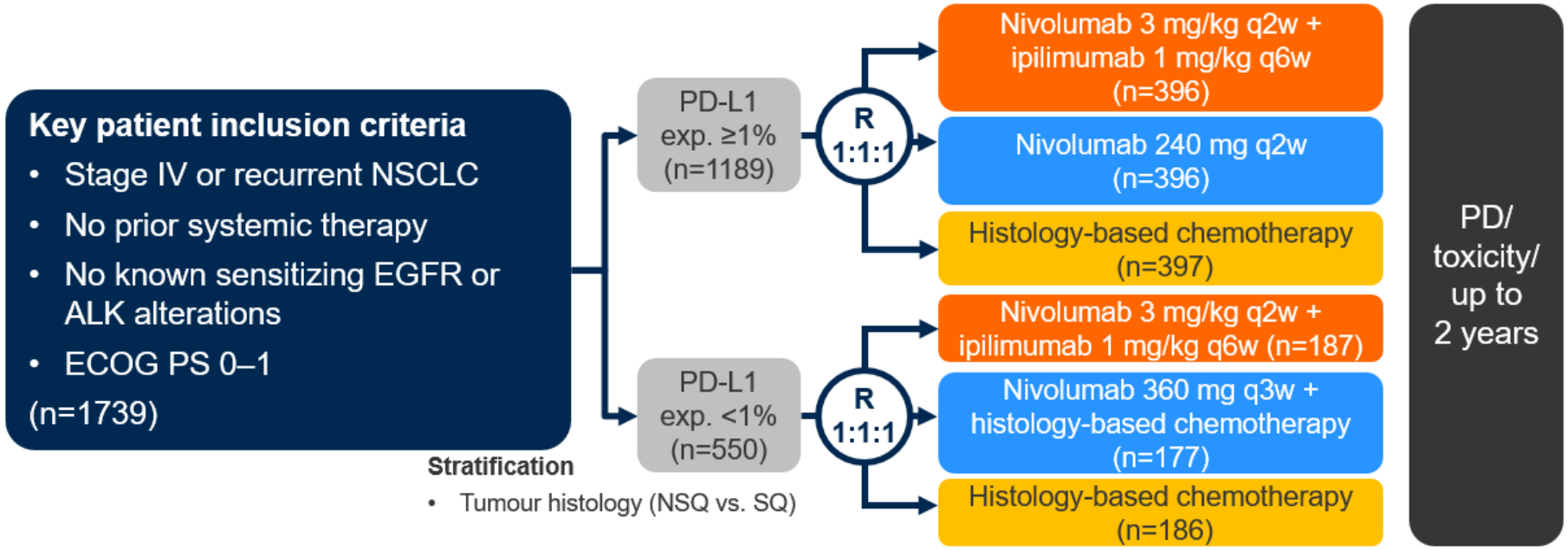
0.25 0.5 1 2 4

NIVO + IPI + chemo ⟷ Chemo

TRAEs 47% vs. 38%

4-year OS CheckMate-227

– To evaluate the longer term efficacy and safety of first-line nivolumab + ipilimumab in patients with advanced NSCLC in CheckMate 227



Primary endpoints

- OS in PD-L1 ≥1% population
- PFS in high TMB (≥10 mut/Mb) population

Secondary endpoints

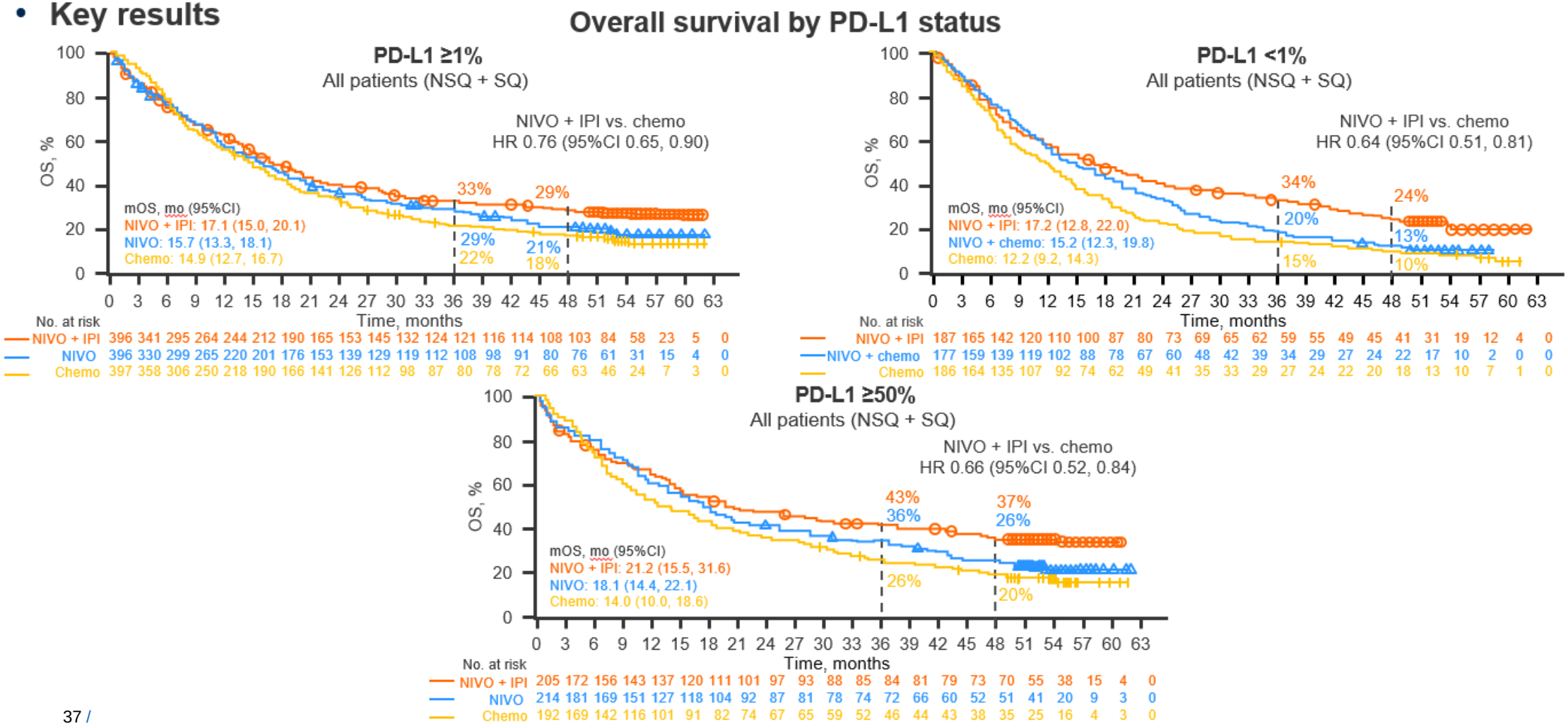
- OS and PFS in patients with PD-L1 expression <1%, OS in patients with PD-L1 ≥50%

Paz-Ares LG, et al. J Clin Oncol 2021;39(suppl):Abstr 9016

Abstract #9016

OS benefit regardless of PD-L1 or histology

- **Key results**



Abstract #9016

CheckMate-9LA and 227

- standard arm no longer in line with current practice (chemo-immuno)
- chemo-immuno or dubble checkpoint inhibition + 2 cycles of chemo?
  - longer follow-up
  - decisions based on histology, PD-L1 expression, co-morbidities , smoking status

Metastatic NSCLC: oncogene addicted

- overcoming osimertinib resistance: promising strategies
- KRAS (G12C)
- updated results for EGFR exon 20, HER2 exon 20, MET, RET

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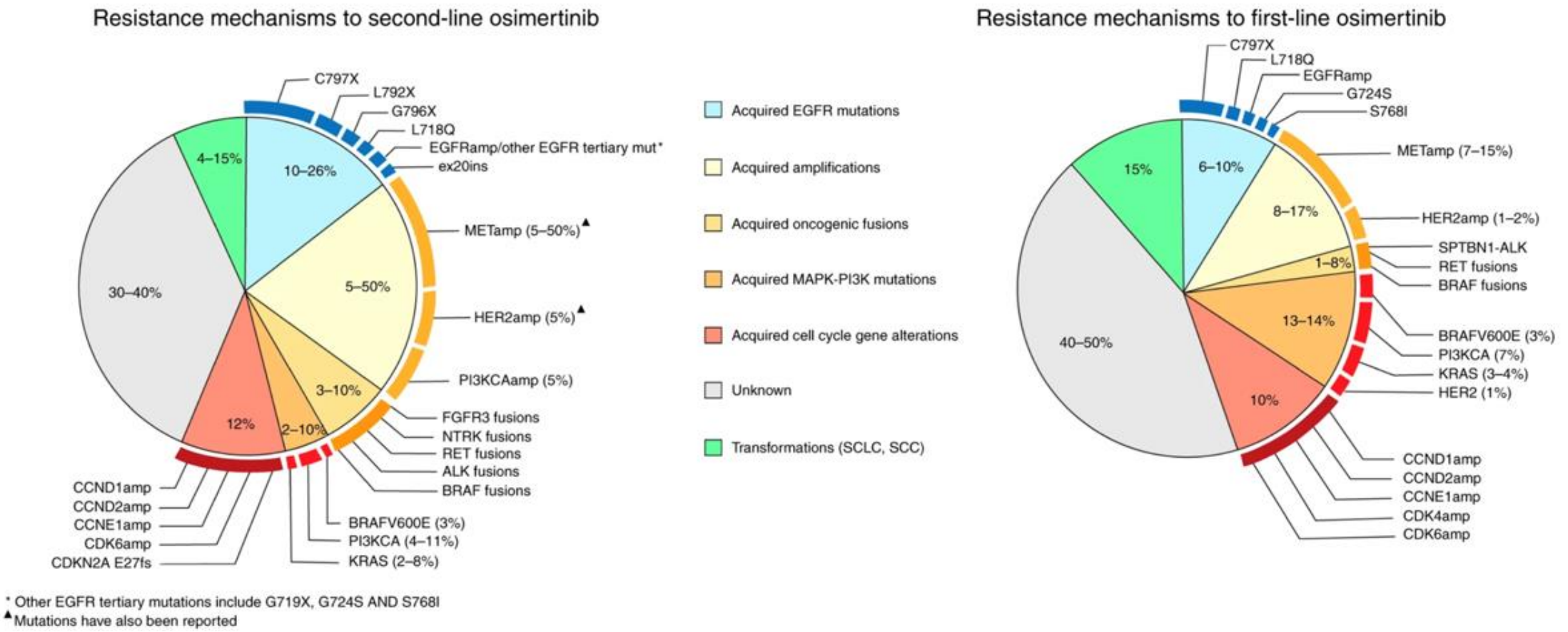
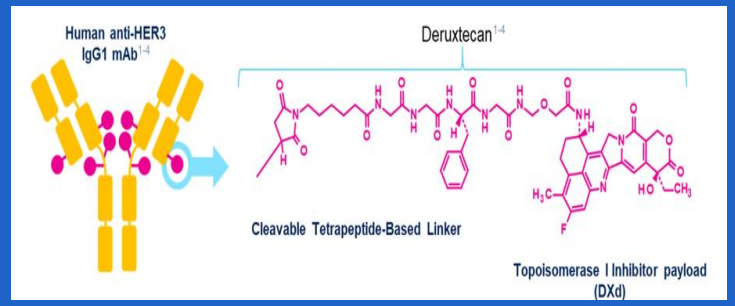
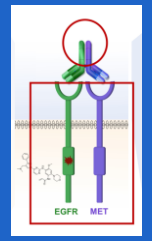
Resistance mechanisms to osimertinib

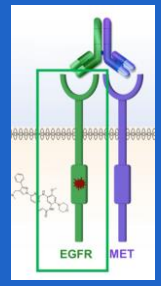


* Other EGFR tertiary mutations include G719X, G724S AND S768I
▲Mutations have also been reported

	Patritumumab-deruxtecan (HER3-DXd) (abstract #9007)	Amivantamab + lazertinib (abstract #9006)
Trial	Phase I dose escalation and expansion	CHRYSALIS phase I dose escalation and expansion
population	EGFR mutation progression on prior TKI	Osimertinib relapsed (n=45)
ORR	39% (26-52)	36% (22-51)
AE	ILD (7%) Platelet count decrease	Rash (78%) Paronychia (49%)

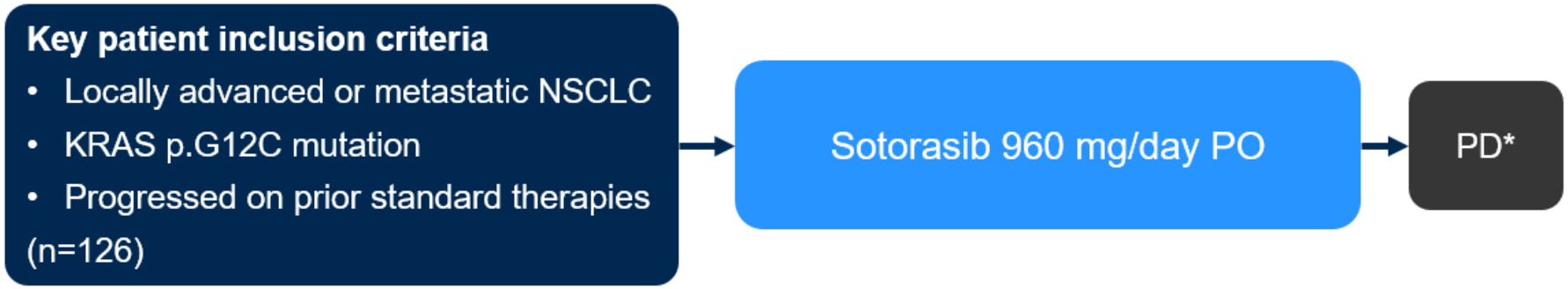






Update and mature OS phase 2 *CodeBreak* 100 trial

- **Study objective**
  - To evaluate the efficacy and safety of sotorasib in previously treated patients with KRAS p.G21C-mutant NSCLC in CodeBreaK 100



Primary endpoint

- ORR (RECIST v1.1, ICR)

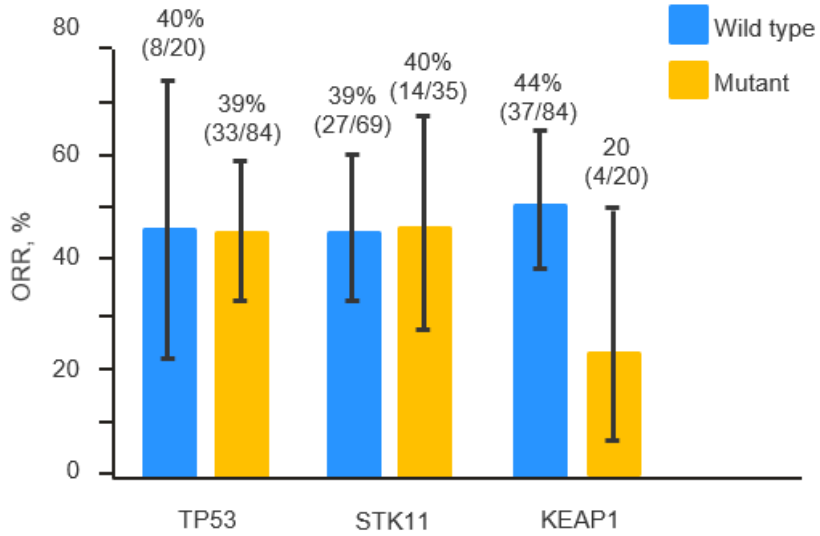
Secondary endpoints

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

Abstract #9003

	Sotorasib 960 mg (n=124)
ORR, % (95%CI)	37.1 (28.6, 46.2)
BOR, n (%)	
CR	4 (3.2)
PR	42 (33.9)
SD	54 (43.5)
PD	20 (16.1)
NE/missing	4 (3.2)
Disease control rate, % (95%CI)	80.6 (72.6, 87.2)
mDoR, months (95%CI)	11.1 (6.9, NE)
Median time to response, months (95%CI)	1.35 (1.2, 10.1)
mPFS, months (95%CI)	6.8 (5.1, 8.2)
mOS, months (95%CI)	12.5 (10.0, NE)

ORR by co-occurring mutations in *TP53, STK11* or *KEAP1* (n=104)



Efficacy in molecular subroups

a phase III trial *CodeBreak 200* sotorasib vs. docetaxel (2/3L) is ongoing

Abstract #9003

Updated results on EGFR exon 20, HER2 exon 20, MET and RET

	EGFR exon 20 (#9014)	HER2 exon 20 (#9015)	MET (#9020)	MET (#9021)	RET (#9089)
agent	Mobocertinib 160 mg QD	Trastuzumab-pertuzumab-docetaxel	Capmatinib 400 mg BID FDA approval EMA awaited	Tepotinib 500 mg QD	Pralsetinib 400 mg QD
ORR	28%	29%	67% (first line) 44% (pretreated)	71% (first line) 42% (pretreated)	62%
mPFS	7.3 m	6.8 m	10.8 m	4.2 m	16.5 m
Tox	TRAEs dis 17%	grade ≥ 3: neutropenia (33%) diarrhea (13%) anemia (9%)	peripheral edema GI effects	grade ≥ 3 TRAEs 29%	TRAEs dis. 6%

SCLC

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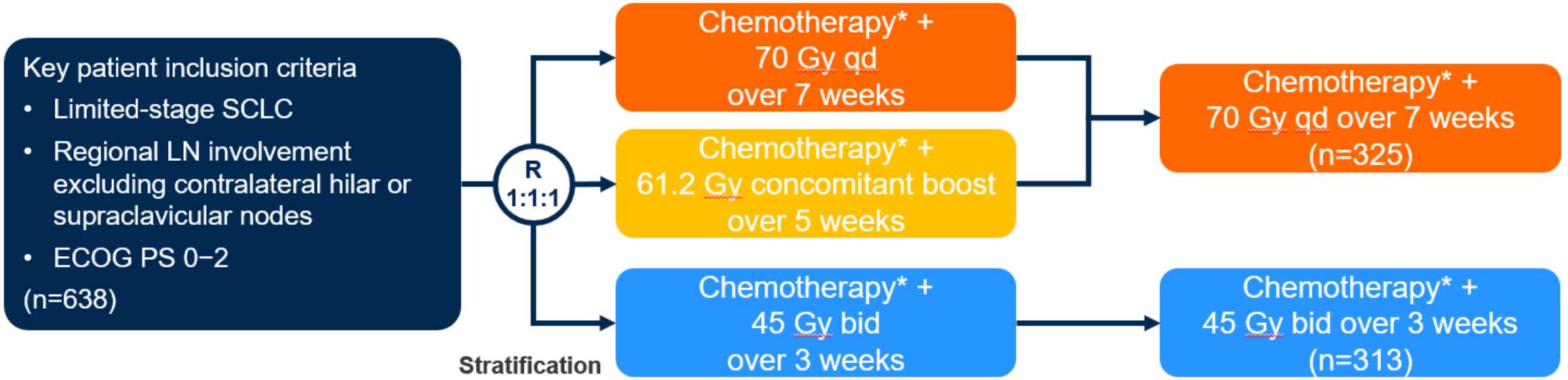
CALGB 30610/RTOG 0538 phase 3 RCT trial

- **Study objective**
  - To evaluate the efficacy of high-dose thoracic radiotherapy (TRT) compared with standard TRT in patients with limited-stage SCLC



Stratification

- Sex, weight loss prior 6 months, ECOG PS, TRT technique (3D vs. IMRT)

Primary endpoint

- OS

Secondary endpoint

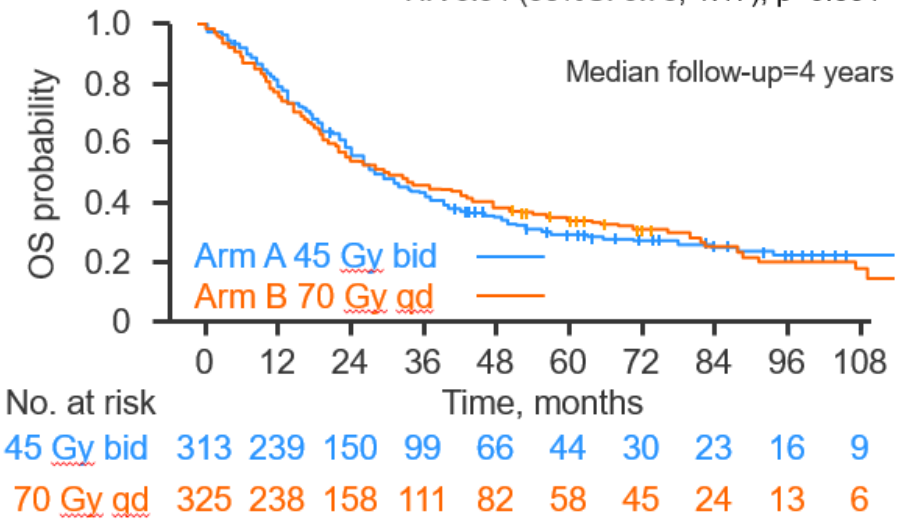
- Safety

Abstract # 8505

Overall survival

	mOS, mo (95%CI)	2-years OS, % (95%CI)	5-years OS, % (95%CI)
45 Gy bid	28.5 (25.4, 35.5)	58 (53, 64)	29 (23, 35)
70 Gy qd	30.5 (25.4, 41.1)	56 (51, 62)	34 (23, 35)

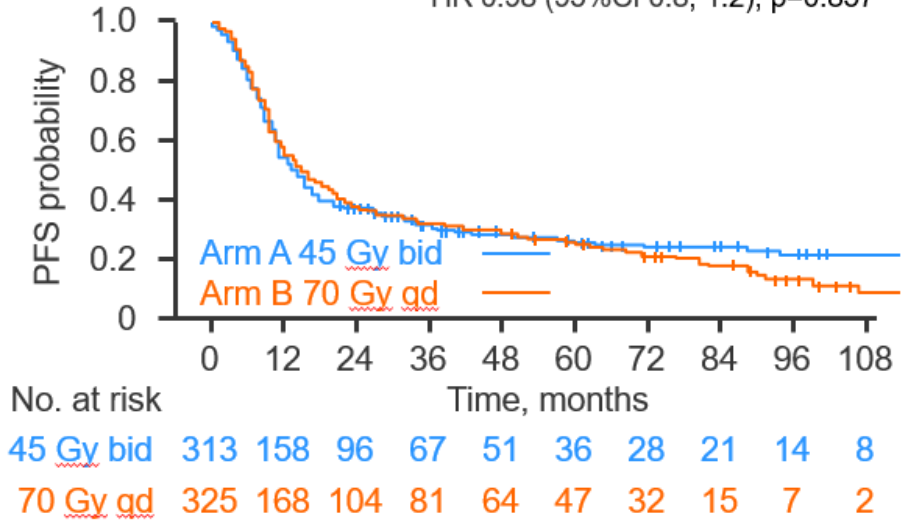
HR 0.94 (95%CI 0.75, 1.17); p=0.591



Progression-free survival

	mPFS, mo (95%CI)	2-years PFS, % (95%CI)	5-years PFS, % (95%CI)
45 Gy bid	13.5 (11.7, 15.8)	36 (31, 42)	25 (20, 31)
70 Gy qd	14.2 (11.9, 17.7)	36 (31, 42)	24 (20, 30)

HR 0.98 (95%CI 0.8, 1.2); p=0.857



45 Gy BID TRT continues to be standard of care

Abstract # 8505

Take home messages

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Early stage

- Atezo (IMpower010):
  - first IC with clinically meaningful benefit (DFS) in adjuvant setting
  - OS needed
  - what in case of relapse?

- Nivo + platinum doublet (CheckMate816):
  - promising
  - more EFS data and OS data needed before practice changing

- TKI for 2 years compared to chemo:
  - DFS advantage, no OS benefit

- VATS lobectomy: standard of care

- SABR vs. VATS in stage IA:
  - PFS and OS not inferior
  - SABR good approach in this population
  - multidisciplinary board decisions

Unresectable stage III

- PACIFIC:
  - first trial improving cure rate (5-y OS)

- trials with IO combinations and RT ongoing

Metastatic non-oncogene addicted first line

- nivo-ipi+ 2 cycles of chemo (CheckMate-9LA)
  - an efficacious 1L treatment
  - we can reduce the number of cycles chemo
- nivo-ipi up to 2 years (CheckMate-227)
- chemo-immuno or dubble checkpoint inhibition + 2 cycles of chemo?

Metastatic: oncogene addicted

- new strategies to overcome osimertinib resistance:
  - HER3-Dxd
  - amivantamab + lazertinib

- KRAS (G12C)
  - sotorasib
  - phase III trial is ongoing (second line)

- new agents for EGFR exon 20, HER2 exon 20, MET exon 14, RET

SCLC (LD)

- high dose 70 Gy once daily vs. standard 45 Gy (BID) RCT phase III trial
  - 45 Gy BID TRT continues to be standard of care