Evolving Role of Immunotherapy in NSCLC

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Objectives

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- Immunotherapy in the advanced stage setting
- Neoadjuvant vs Adjuvant Immunotherapy
- Safety

Lung Cancer: the big picture

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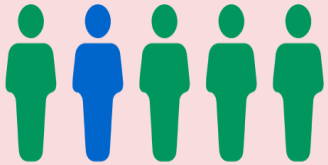
Lung cancer is the **most common cancer** in the world[1]

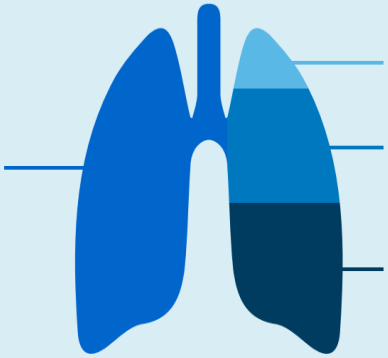
1 in 5 of all cancer deaths



Worldwide, **three people die** from lung cancer **every minute**[2]

Lung cancer is responsible for **more cancer-related deaths** than prostate, breast and colorectal cancer combined[3]

Lung cancer: **1,590,000 deaths**



Prostate cancer: 307,000 deaths

Breast cancer: 522,000 deaths

Colorectal cancer: 694,000 deaths

1. Cancer Research UK. http://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwide-cancer#heading-Three;
2. WHO. http://www.who.int/mediacentre/factsheets/fs297/en/; 3. GLOBOCAN. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx

Lung Cancer is a Heterogeneous Disease

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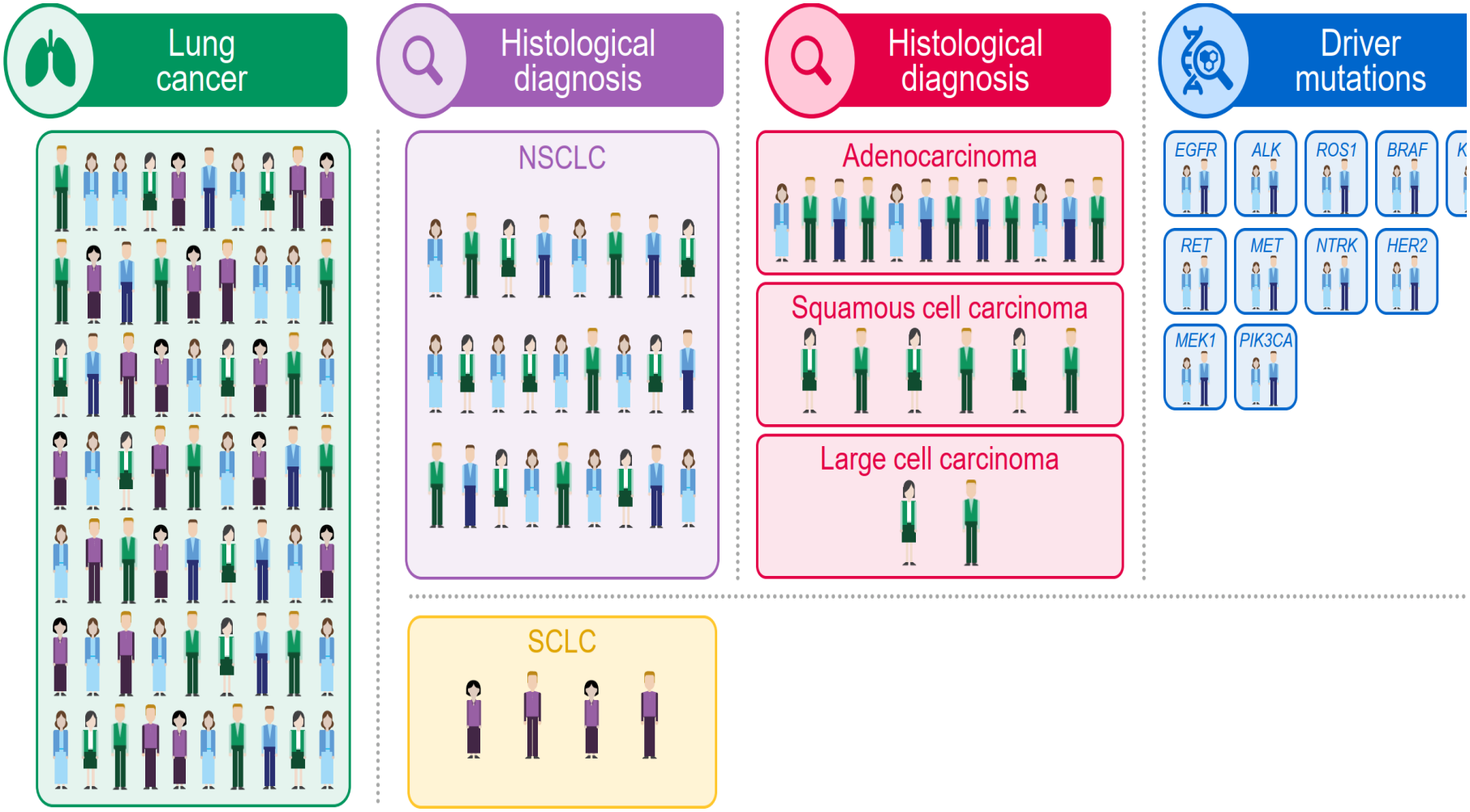

Reck, et al. Lancet 2013; Shukuya and Carbone. J Thorac Oncol 2016; Planchard, et al. Ann Oncol 2018

Evolving Treatment Landscape

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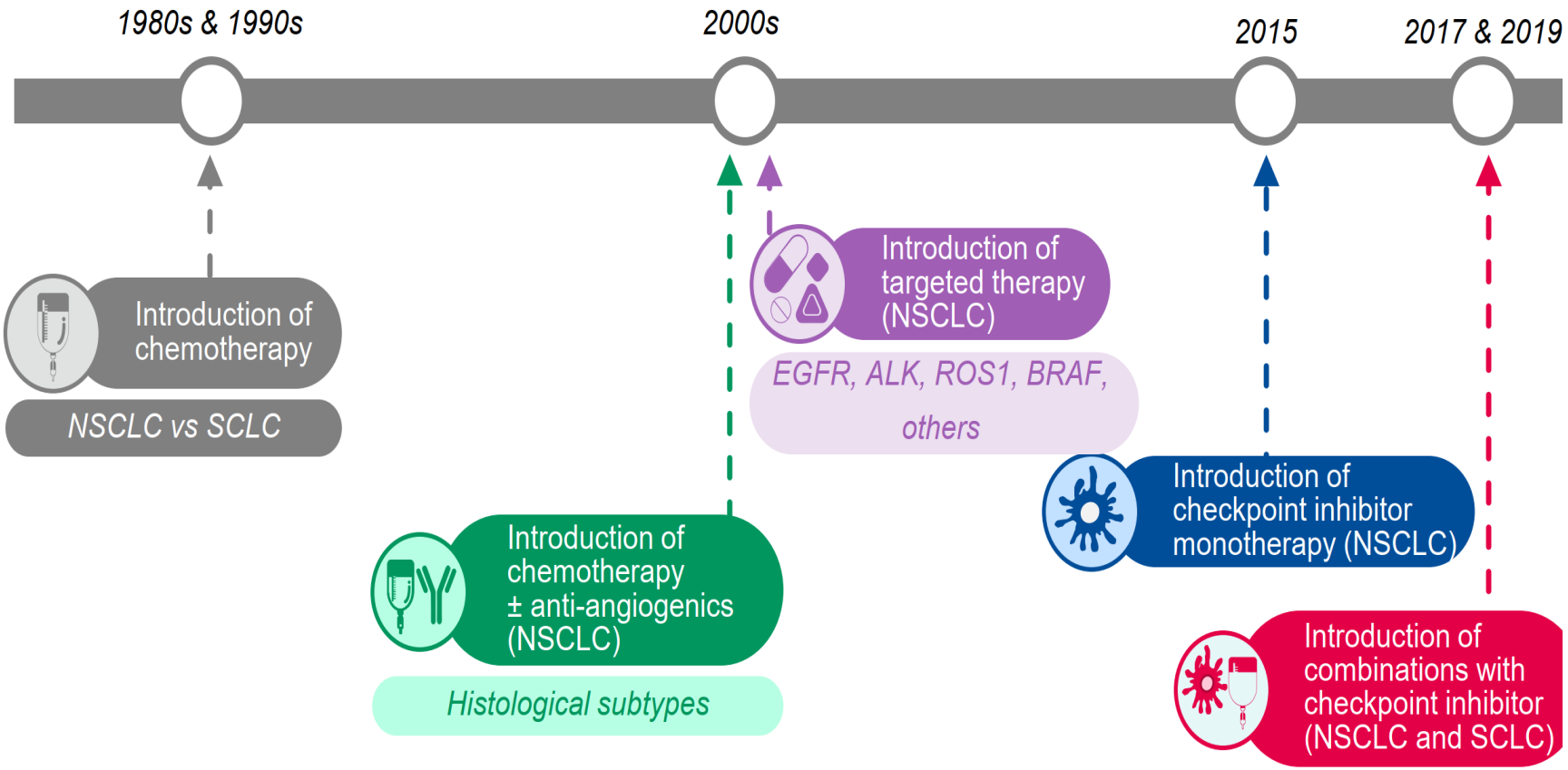

Bunn, Semin Oncol 1989; Bunn, et al. Clin Cancer Res 1998; Scagliotti, et al. J Clin Oncol 2002; Sandler, et al. N Engl J Med 2006 Shepherd, et al. N Engl J Med 2005; Brahmer, et al. N Engl J Med 2015; Socinski, et al N Engl J Med 2018; Horn, et al. N Engl J Med 2018

How do you choose which regimen to use?

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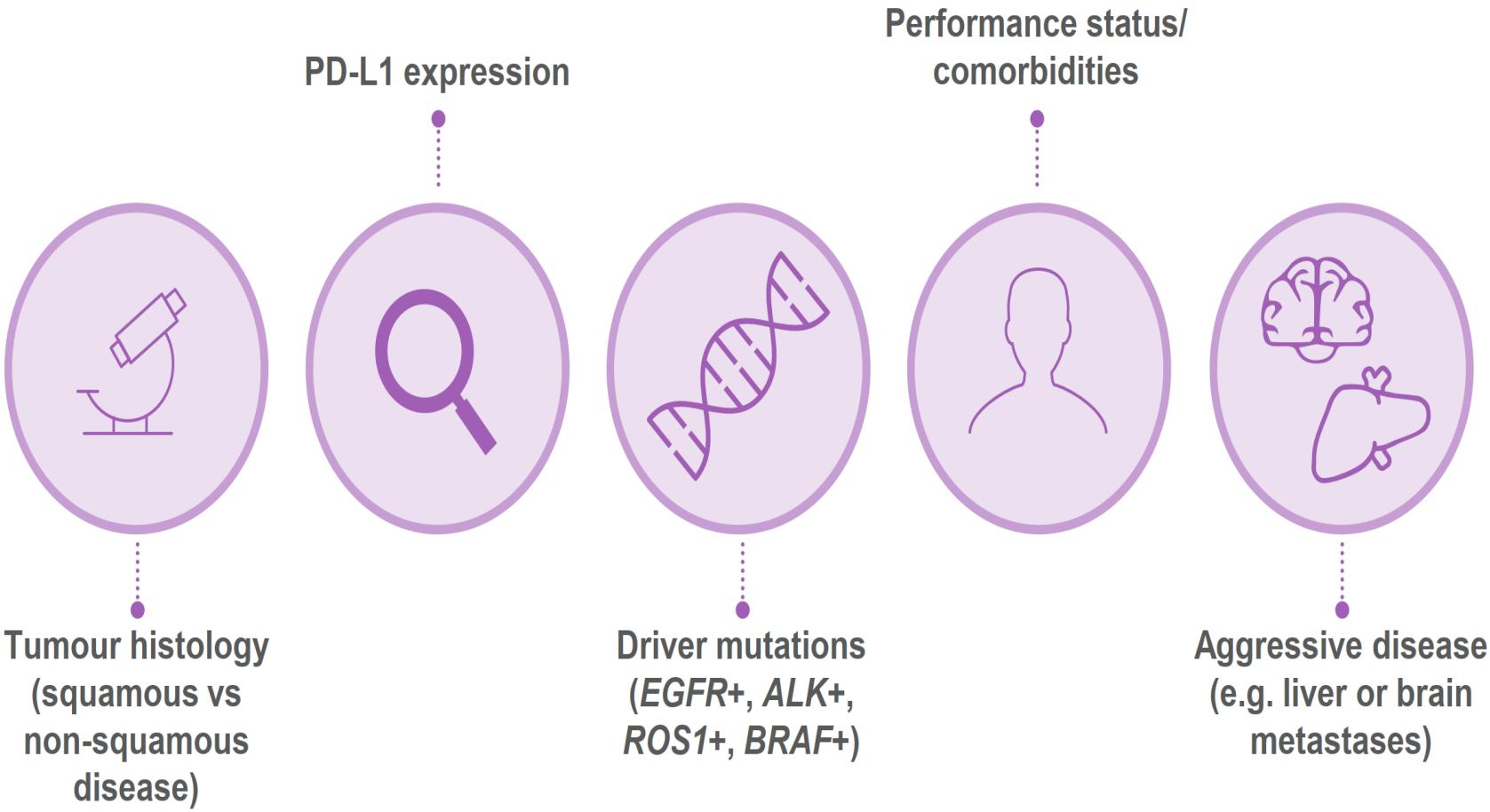

How to choose the best therapy in Stage IV NSCLC

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- Does the patient have a driver?
  - If yes → targeted therapy

How to choose the best therapy in Stage IV NSCLC

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- Does the patient have a driver?
  - If yes → targeted therapy
  - If no:

- Is the patient a candidate for immunotherapy?
  - If no → standard chemotherapy

Standard of Care in Patients with Drivers and not Candidates for Immunotherapy

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- Non-squamous
  - Platinum plus pemetrexed or taxane doublets
  - Bevacizumab in selected patients
  - 4 cycles plus maintenance (pemetrexed/bevacizumab)
- Squamous
  - Platinum plus taxane or gemcitabine
  - 4 cycles
  - No role for maintenance

How to choose the best therapy in Stage IV NSCLC

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- Does the patient have a driver?
  - If yes → targeted therapy
  - If no:
- Is the patient a candidate for immunotherapy?
  - If no → standard chemotherapy
  - If yes:
- Is the patient a candidate for single-agent immunotherapy?
  - If yes → Keynote-024, IMpower110 & EMPOWER-Lung-01

KN 24 Pembrolizumab vs Chemotherapy in PD-L1 High (≥50%) NSCLC

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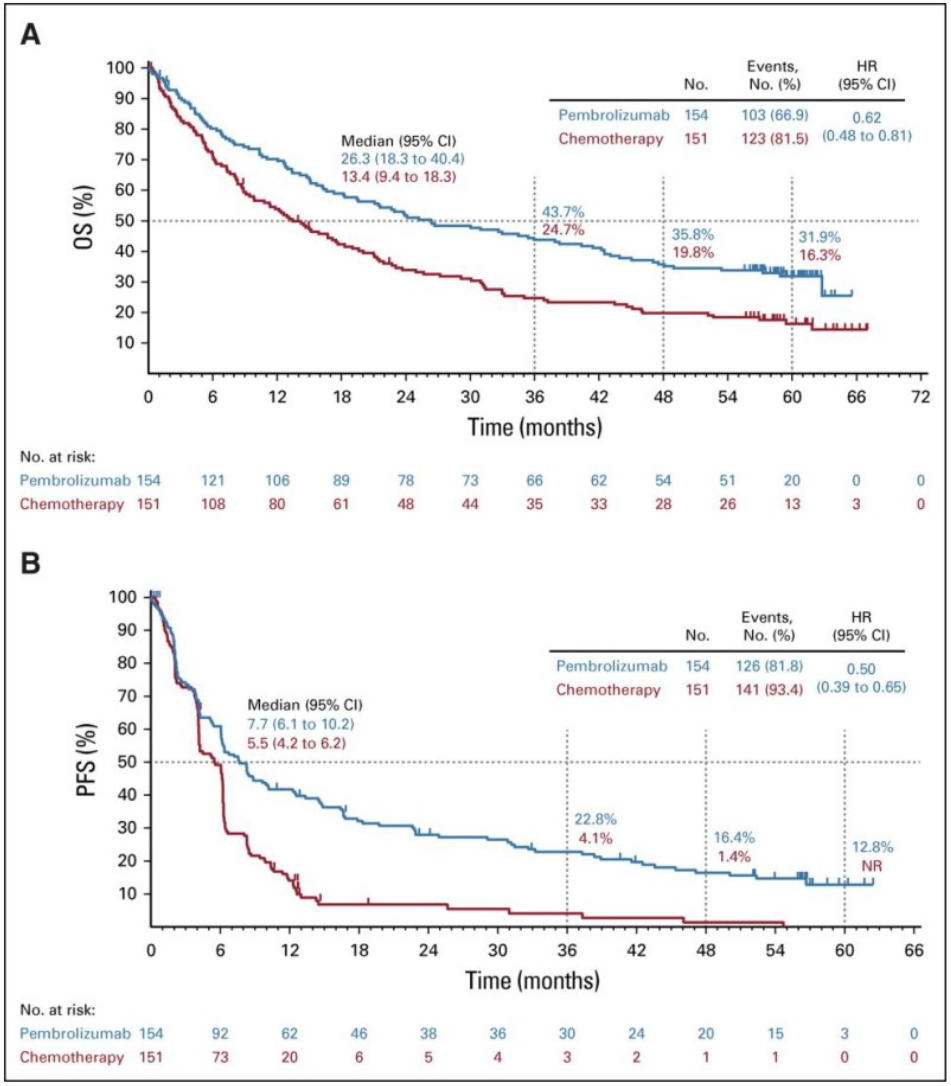

Reck et al. JCO 2021

IMpower 110: Atezolizumab v Chemo OS in TC3 or IC3

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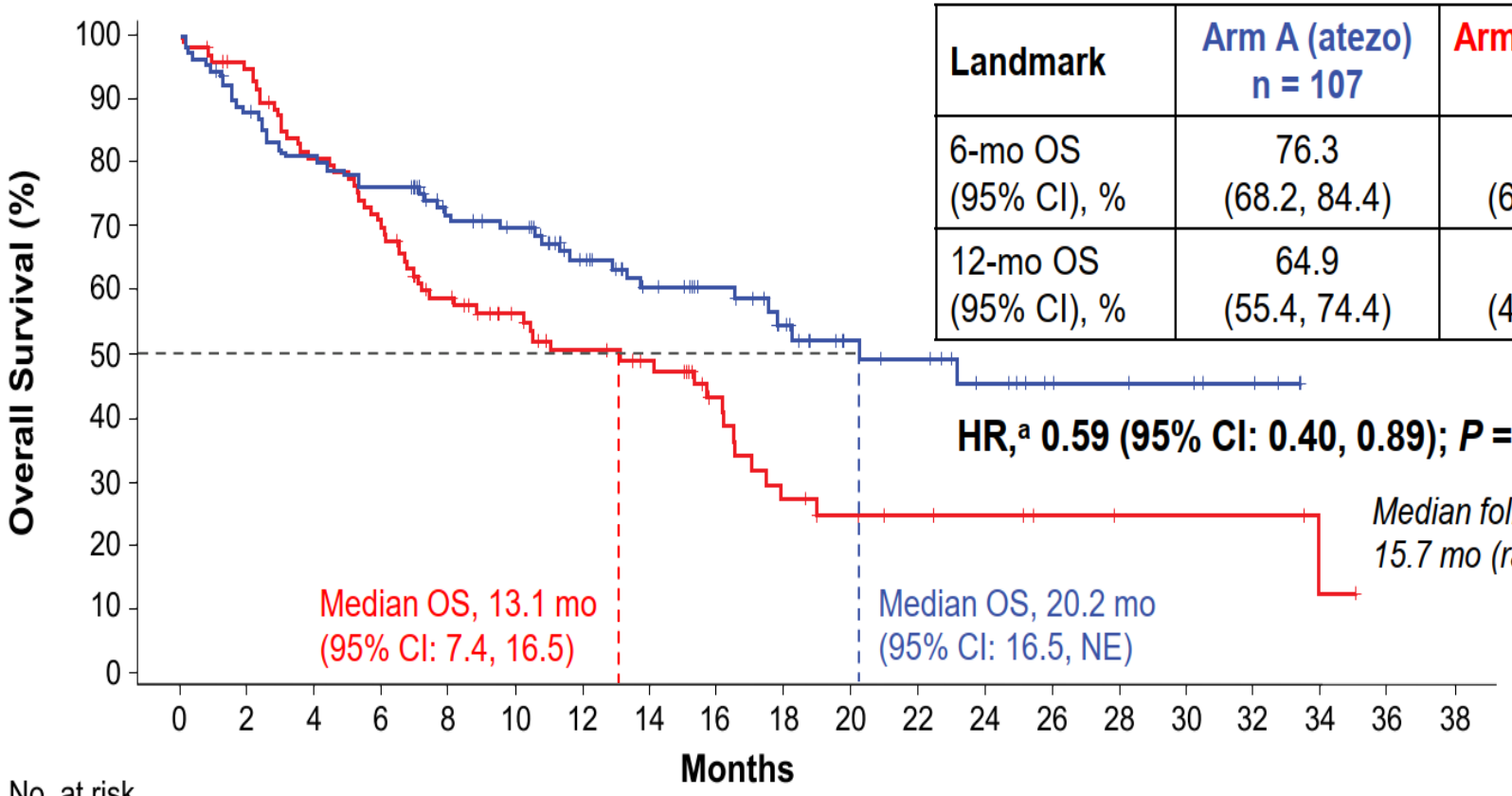

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)

No. at risk

Atezolizumab	107	94	85	80	66	61	48	40	34	25	18	16	11	7	6	5	2
Chemotherapy	98	89	75	65	50	40	33	28	19	12	9	7	6	4	3	3	3	1

NE, not estimable. [a] Stratified. [b] Stratified log-rank.
Data cutoff: 10 September 2018.

Spigel ESMO 2019

EMPOWER-Lung-1: Cemiplimab v Chemo in PD-L1 ≥ 50% NSCLC

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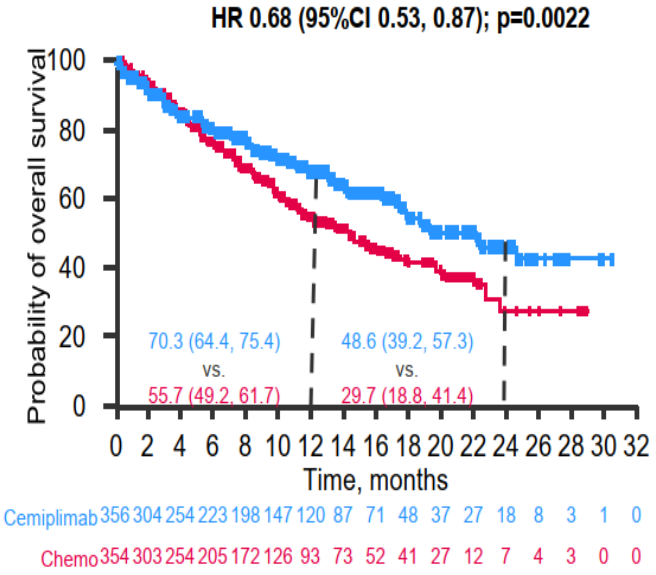
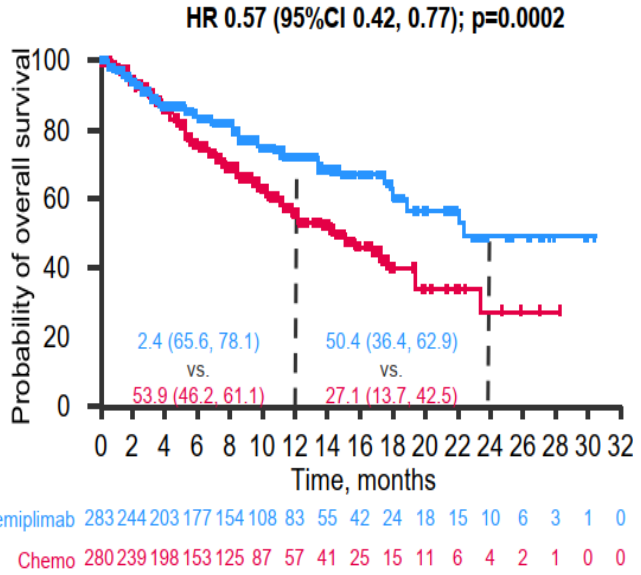
ITT (PD-L1 ≥50%)

	No. of patients	Median OS, mo (95%CI)
Cemiplimab	356	22.1 (17.7, NE)
Chemotherapy	354	14.3 (11.7, 19.2)



PD-L1 ≥50%-confirmed ITT

	No. of patients	Median OS, mo (95%CI)
Cemiplimab	283	NR (17.9, NE)
Chemotherapy	280	14.2 (11.2, 17.5)



Sezer A, et al. Ann Oncol 2020;31(suppl):Abstr LBA52

OS Results in RCTs comparing ICI to Chemo in PD-L1 High NSCLC

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Trial	Agent	N	OS HR
Keynote 024	Pembrolizumab	305	0.62
Keynote 042 (≥ 50%)	Pembrolizumab	599	0.69
IMPower 110 TC3/IC3	Atezolizumab	205	0.59
EMPOWER-Lung-1	Cempilimab	563	0.57

OS Results in RCTs comparing ICI to Chemo in PD-L1 High NSCLC

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IMPower 110 TC3/IC3	Atezolizumab	205	0.59
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- Acceptable standard in high PD-L1 expressors particularly very high expression (≥ 90%)
- May not be optimal for all high expressors (symptomatic, high tumor burden etc)

How to choose the best therapy in Stage IV NSCLC

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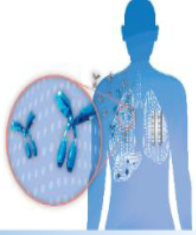
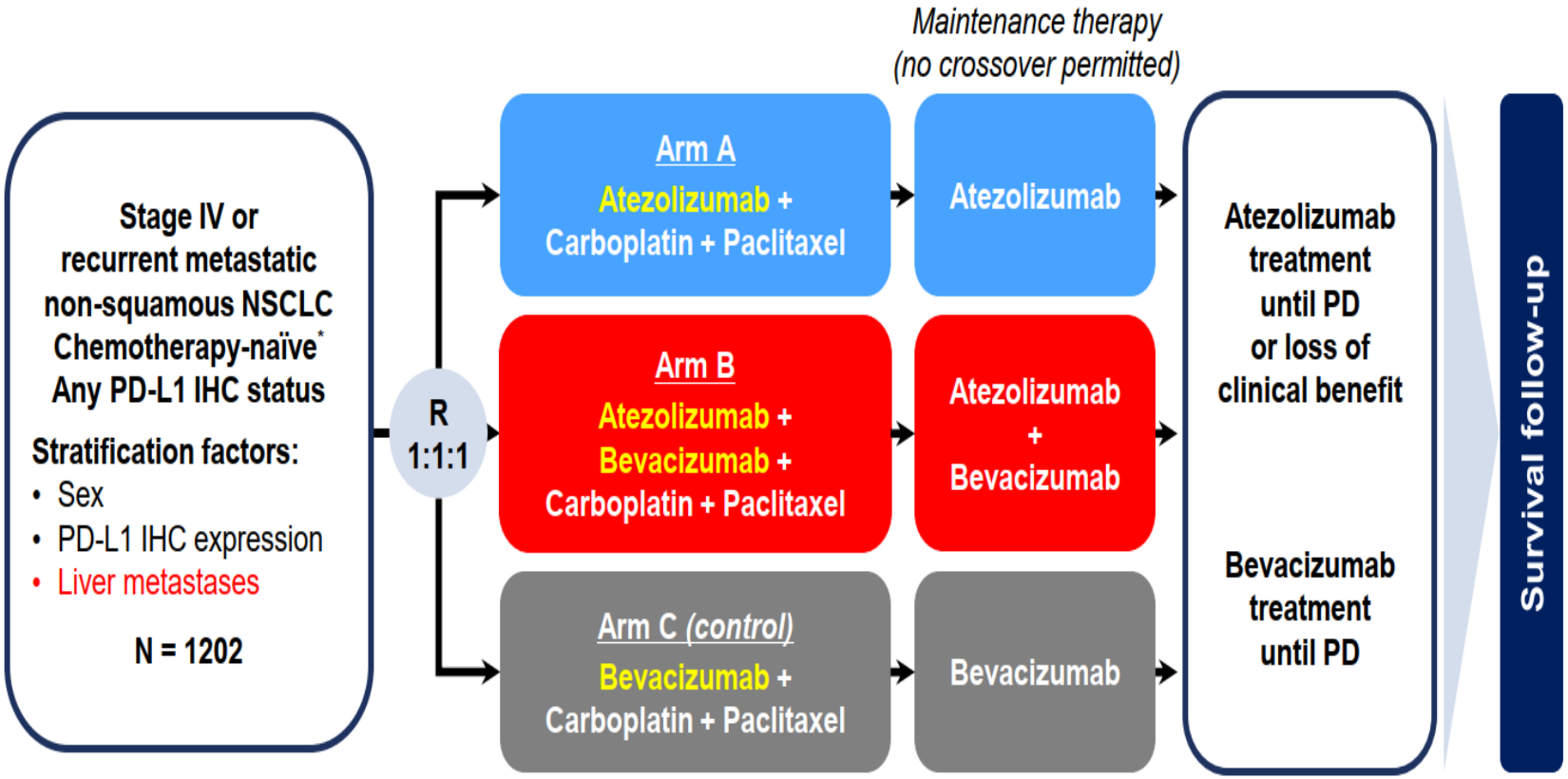
- Does the patient have a driver?
  - If yes → targeted therapy
  - If no:

- Is the patient a candidate for immunotherapy?
  - If no → standard chemotherapy
  - If yes:

- Is the patient a candidate for single-agent immunotherapy?
  - If yes → Keynote-024, Impower 110 & EMPOWER-Lung-01
  - If no → Keynote-189, Keynote-407, IMpower 150, IMpower 130, IMpower 131, IMpower 132, EMPOWER-Lung-03, ……

IMpower150: a phase III global trial which stratified for liver metastases at randomisation





*Patients with a sensitising *EGFR* mutation or *ALK* translocation must have disease progression or intolerance to treatment with one or more approved targeted therapies

Socinski, et al. N Engl J Med 2018

IMpower 150 met its OS and PFS endpoints

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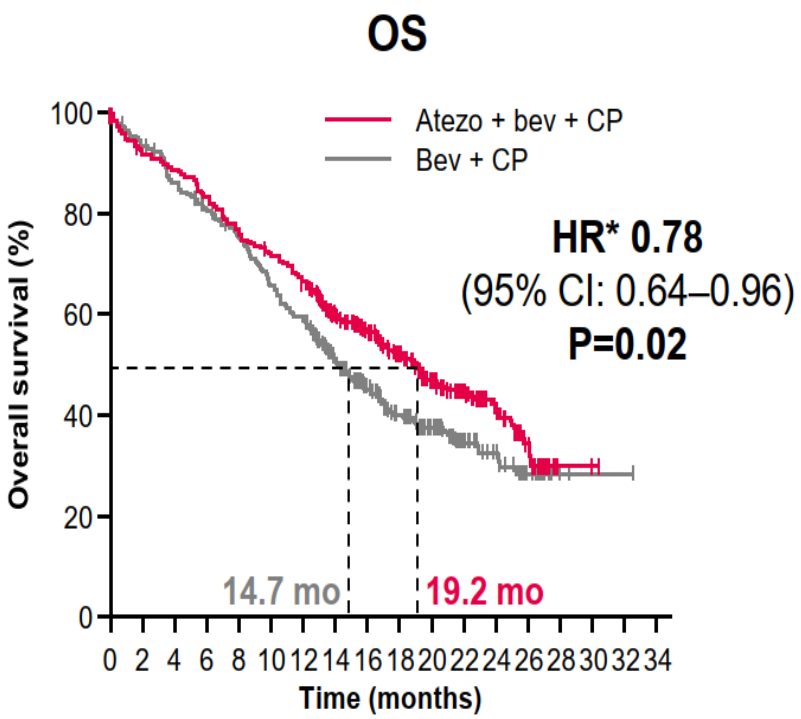
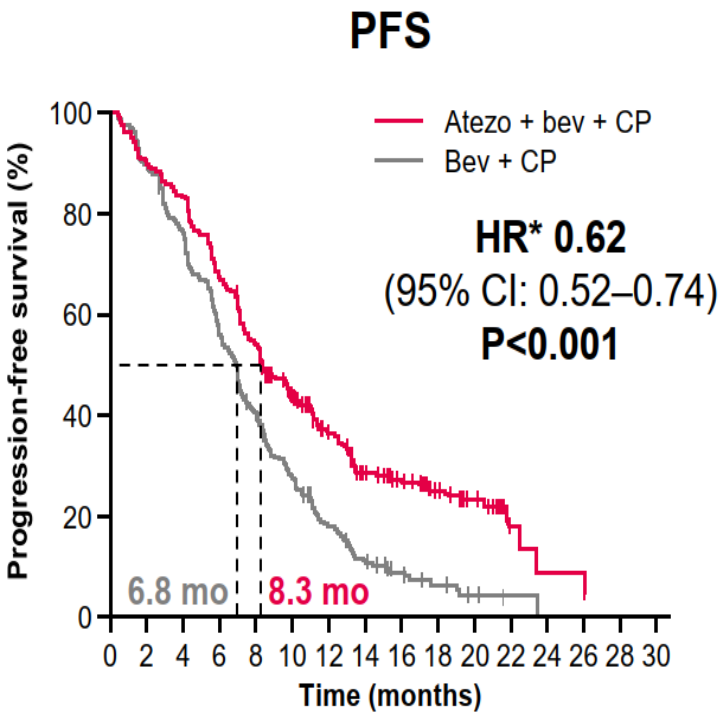


Minimum follow-up: ~14 mo
Median follow-up: ~20 mo



Minimum follow-up: 9.5 mo
Median follow-up: ~15 mo

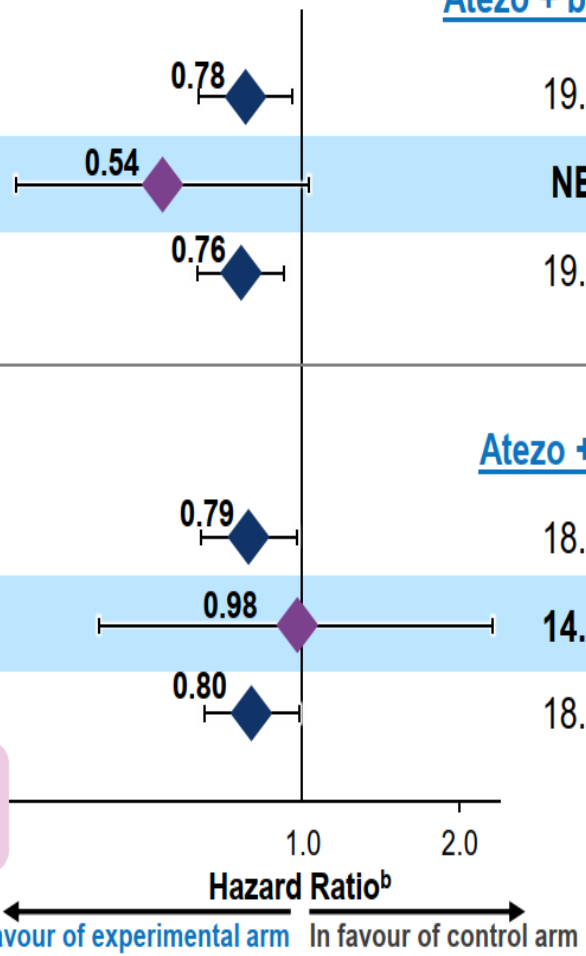
*Stratified HR. Data cut-off: 22 January 2018 (OS); 15 September 2017 (PFS)

Socinski, et al. N Engl J Med 2018

EGFR+/*ALK*+ subgroup data from other first-line atezolizumab trials in NSCLC

	Subgroup	n (%)	Median OS, mo: Atezo + bev + CP	Median OS, mo: Bev + CP
	ITT-WT	696 (87%)	19.2	14.7
IMpower150[1]	***EGFR*+/*ALK*+ only**	**104[a] (13%)**	**NE**	**17.5**
	ITT (including *EGFR*+/*ALK*+)	800 (100%)	19.8	14.9

	Subgroup	n (%)	Atezo + CnP	CnP
	ITT-WT	679 (94%)	18.6	13.9
IMpower130[2]	***EGFR*+/*ALK*+ only**	**44 (6%)**	**14.4**	**10.0**
	ITT (including *EGFR*+/*ALK*+)	723 (100%)	18.1	13.9



Analyses from IMpower130 further supports the role of anti-VEGF therapy and CIT in patients with *EGFR*+/*ALK*+ NSCLC

Data cut-off for IMpower150: 22 January, 2018.
Data cut-off for IMpower130: 15 March, 2018.
[a]One patient had *EGFR* exon 19 deletion and also tested *ALK* positive per central lab. [b]Stratified HR for ITT populations, unstratified HRs for subgroups.

Socinski et al. ASCO 2018 (9002); Cappuzzo et al. ESMO 2018 (LBA53)

KN189 – OS by PD-L1 TPS

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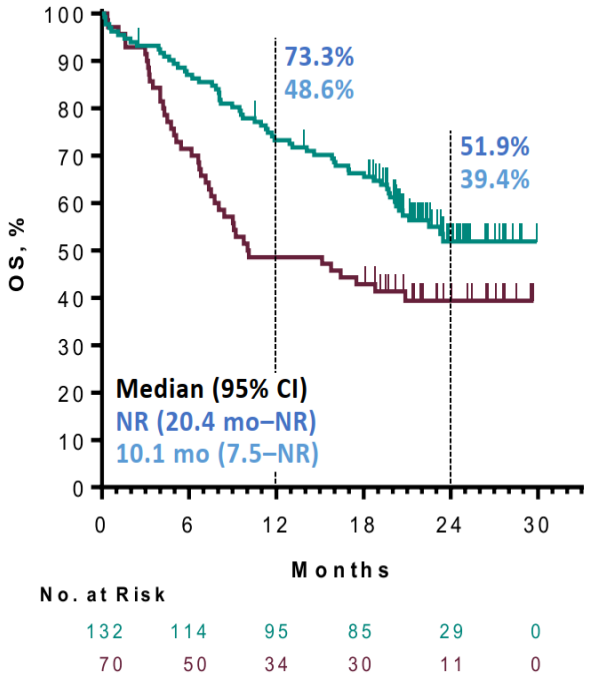
KN 189- OS by PD-L1 TPS

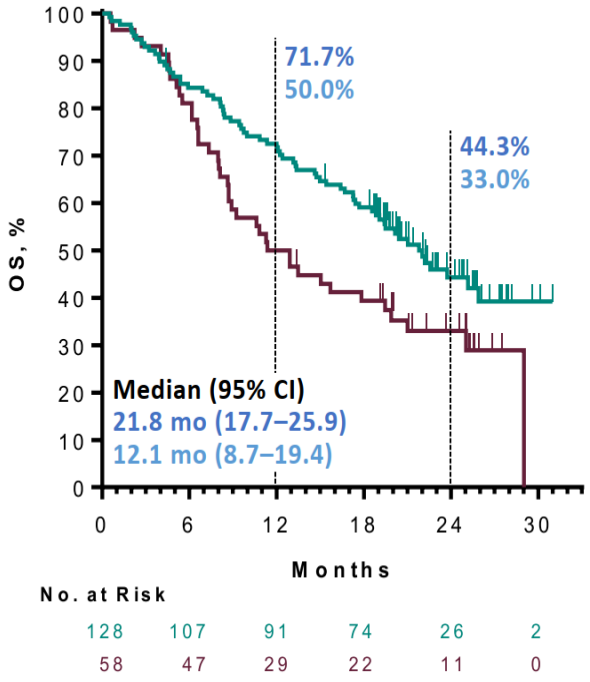
TPS ≥50 %

	Events	HR (95% CI)
Pembro/Pem/Plat	43.9%	0.59 (0.39–0.88)
Placebo/Pem/Plat	60.0%	



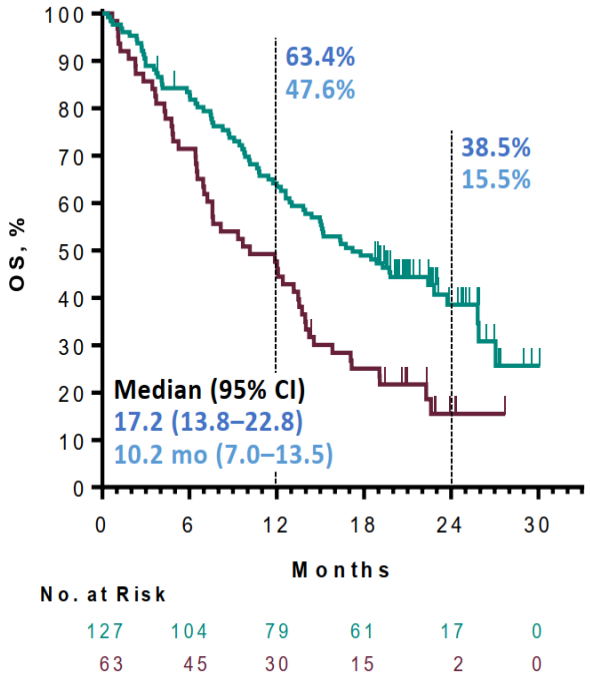
TPS 1-49%

	Events	HR (95% CI)
Pembro/Pem/Plat	52.3%	0.62 (0.42–0.92)
Placebo/Pem/Plat	69.0%	



TPS <1%

	Events	HR (95% CI)
Pembro/Pem/Plat	59.1%	0.52 (0.36–0.74)
Placebo/Pem/Plat	81.0%	



Data cutoff date: Sep 21, 2018.

Gadgeel S et al. J Clin Oncol 2021.

Adding IO to Chemotherapy Regimens in NSCLC

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Trial	Control	Histology	mOS Control/Inv	HR
KN-189	CbPem	NSq	10.6/22	0.60
KN-407	CbTaxane	Sq	11.3/15.9	0.64
IMP-150	CbPacBev	NSq	14.7/19.2	0.80
IMP-130	CbnabPac	NSq	13.9/18.6	0.79
IMP-131	CbnabPac	Sq	13.5/14.2	0.88
IMP-132	PlatPem	NSq	13.6/17.5	0.86
EMPOWER-3	PlatPem or PlatTaxane	NSCLC	12.9/21.1	0.65

Adding IO to Chemotherapy Regimens in NSCLC

INOVA Schar Cancer Institute

Trial	Control	Histology	mOS Control/Inv	HR
KN-189	CbPem	NSq	10.6/22	0.60
KN-407	CbTaxane	Sq	11.3/15.9	0.64
IMP-150	CbPacBev	NSq	14.7/19.2	0.80
IMP-130	CbnabPac	NSq	13.9/18.6	0.79
IMP-131	CbnabPac	Sq	13.5/14.2	0.88
IMP-132	PlatPem	NSq	13.6/17.5	0.86
EMPOWER-Lung 3	PlatPem or PlatTaxane	NSCLC	12.9/21.1	0.65

- Selecting single agent IO vs chemoIO high expressor depends on
  - tumor volume & symptoms
- Where do IO-IO combinations fit in?
  - Checkmate 227, Checkmate 9LA, POSEIDON, Keynote 598

Where do IO-IO combinations fit in?

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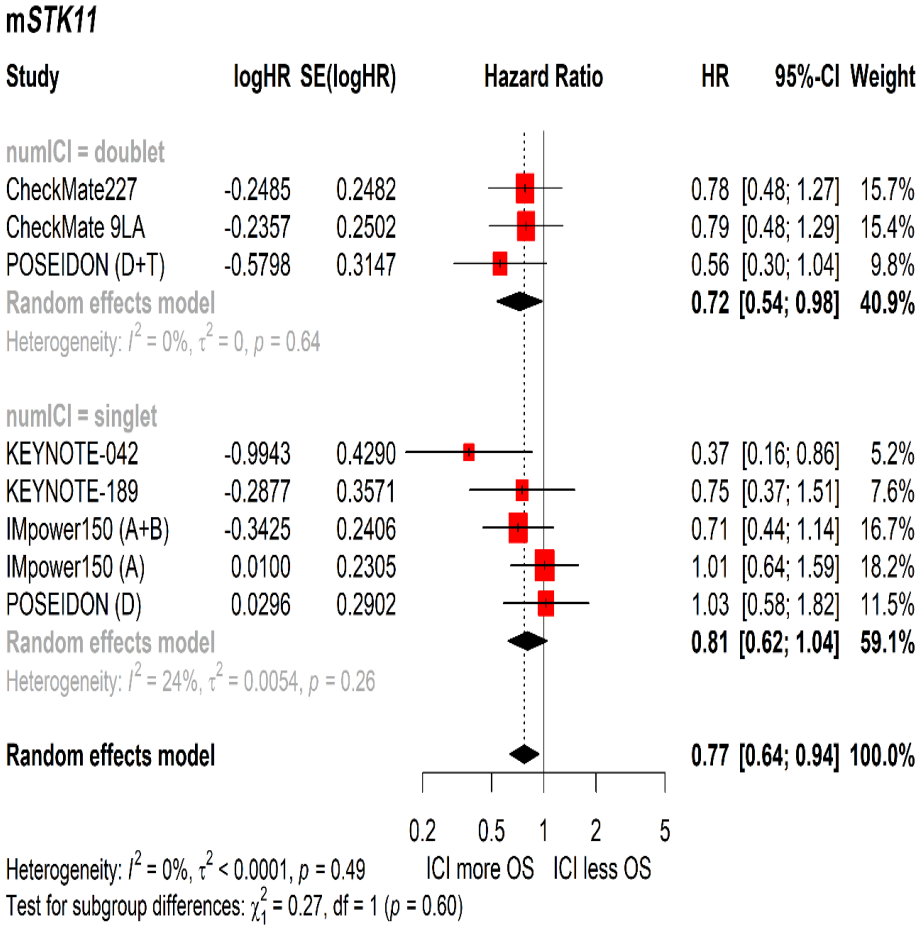

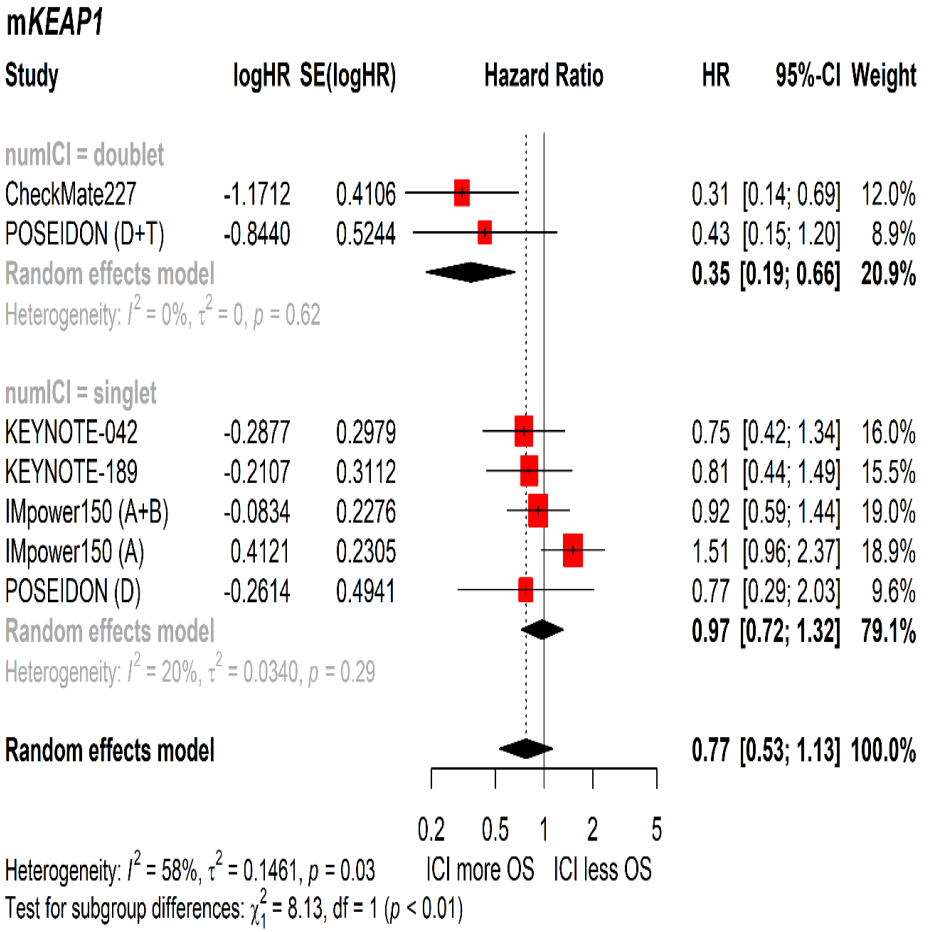

Ponvilawan B, Subramanian J et al. JTO 2023 (in press)

Where do IO-IO combinations fit in?

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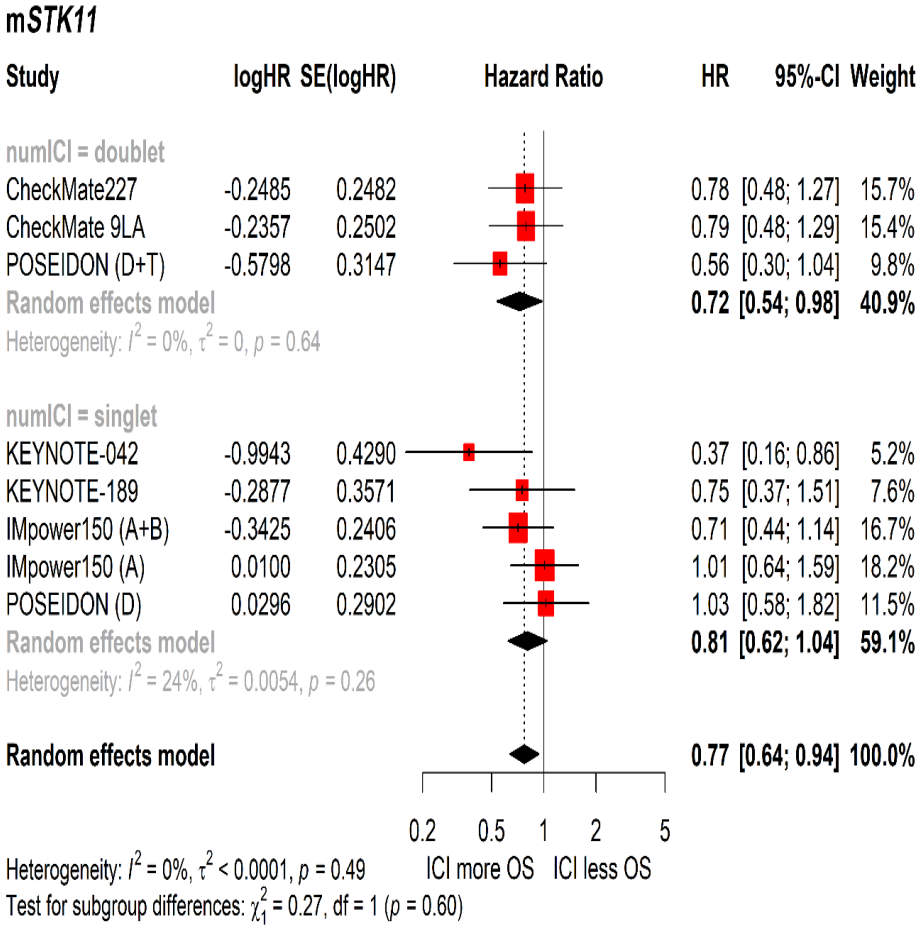
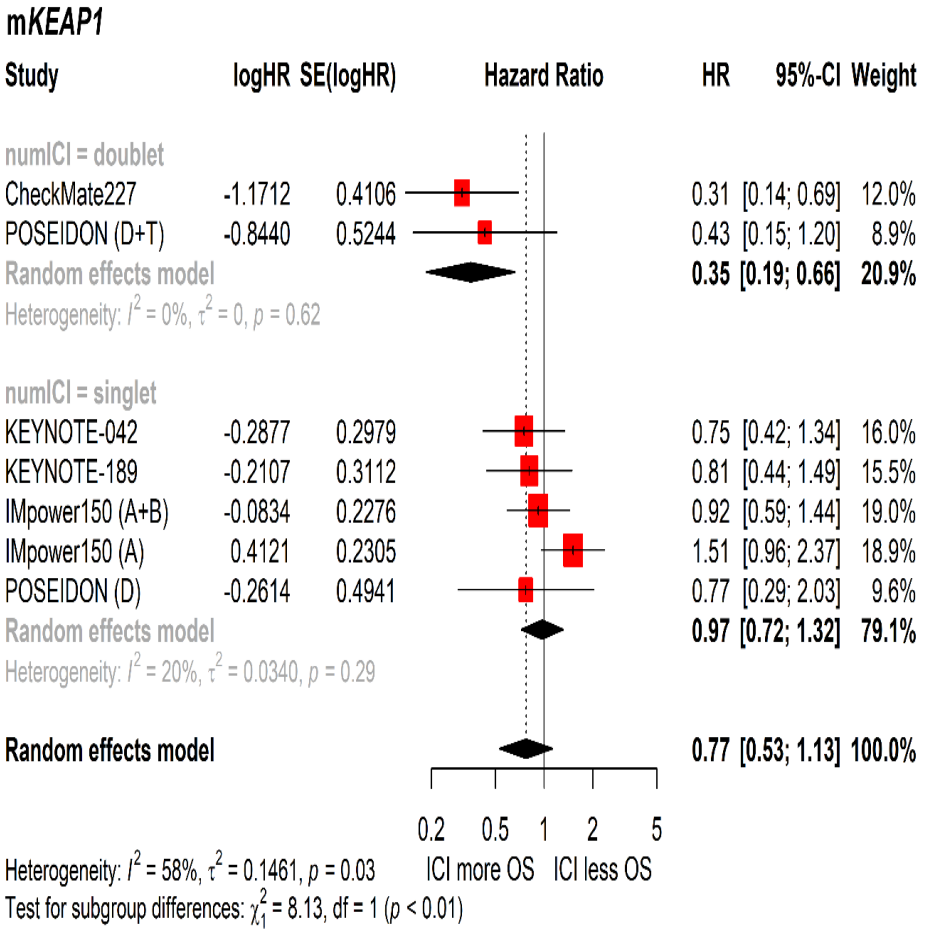




- Possibly KRAS commutated STK11/KEAP1
- Chemotherapy intolerant → Checkmate 227

Ponvilawan B, Subramanian J et al. JTO 2023 (in press)

Locally Advanced NSCLC

PACIFIC: Study Design

Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study[1]

- Unresectable, Stage III NSCLC without progression after definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumor tissue for PD-L1 testing*

All-comers population (i.e. irrespective of PD-L1 status)

N=713 randomized

1–42 days post-cCRT

R

2:1 randomization, stratified by age, sex, and smoking history

Durvalumab 10 mg/kg q2w for up to 12 months N=476

Placebo 10 mg/kg q2w for up to 12 months N=237

Primary endpoints

- PFS by BICR using RECIST v1.1†
- OS

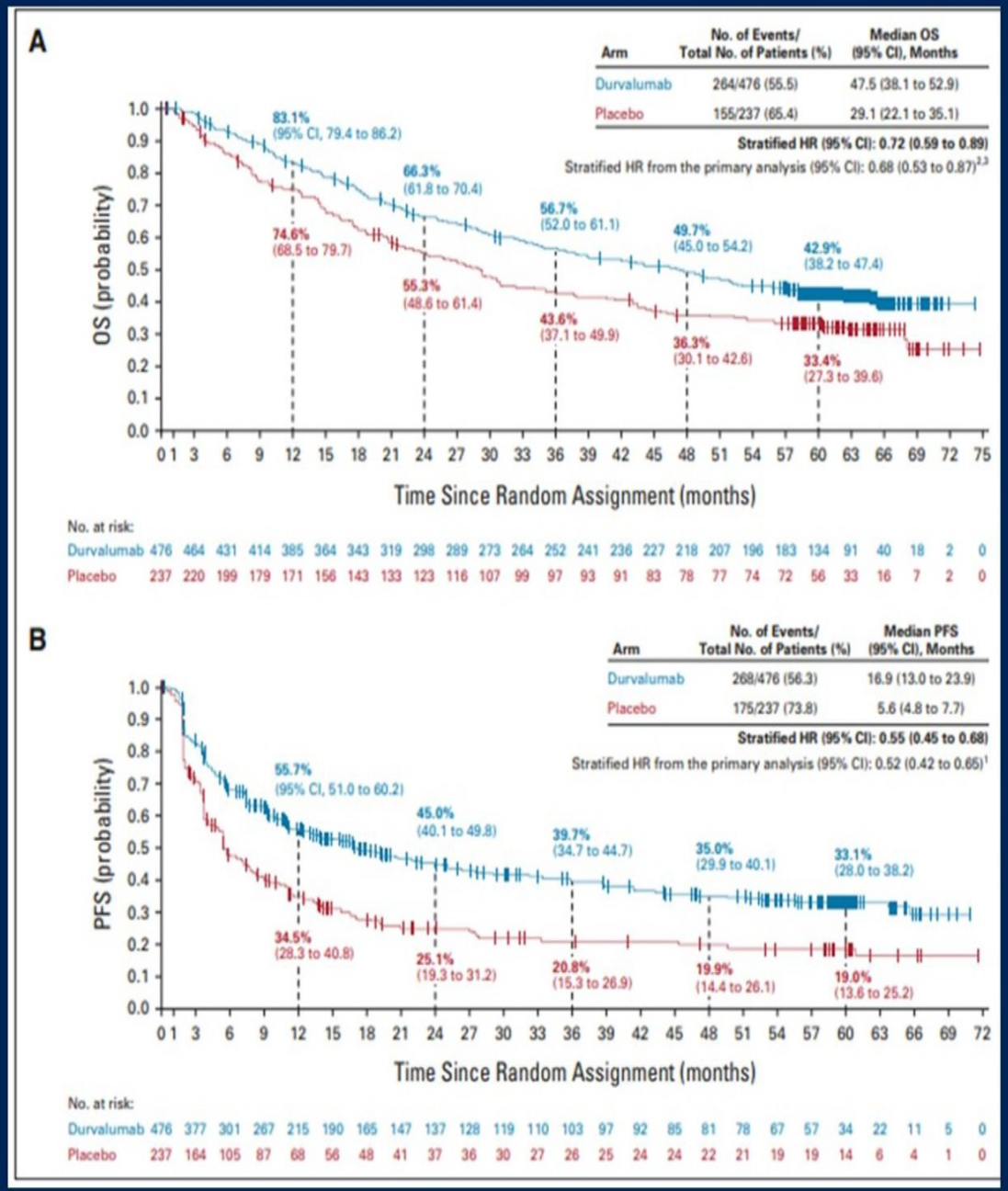
Key secondary endpoints

- ORR, DoR and TTDM by BICR
- PFS2 by investigator
- Safety
- PROs

*Using the Ventana SP263 immunohistochemistry assay

†Defined as the time from randomization until the date of objective disease progression or death by any cause in the absence of progression. BICR, blinded independent central review; cCRT, concurrent CRT; PFS2, time to second progression; RECIST, Response Evaluation Criteria in Solid Tumors; TTDM, time to death or distant metastasis. ClinicalTrials.gov number: NCT02125461

PACIFIC TRIAL



HR = 0.72 OS

Median 47.5 vs 29.1mn

HR = 0.55 PFS

Median 16.9 vs 5.6 mn

Entry Criteria

- No progression during the course of CHEMO/RT
- No unresolved > Grade 2 toxicities
- No Grade ≥ 2 Pneumonitis

Updated Safety Summary

	Durvalumab (N=475)	Placebo (N=234)
Any-grade all-causality AEs, n (%)	460 (96.8)	222 (94.9)
Grade 3/4	145 (30.5)	61 (26.1)
Outcome of death	21 (4.4)	15 (6.4)
Leading to discontinuation	73 (15.4)	23 (9.8)
Serious AEs, n (%)	138 (29.1)	54 (23.1)
Any-grade pneumonitis/radiation pneumonitis, n (%)	161 (33.9)	58 (24.8)
Grade 3/4	17 (3.6)	7 (3.0)
Outcome of death	5 (1.1)	5 (2.1)
Leading to discontinuation	30 (6.3)	10 (4.3)

Durvalumab Consolidation

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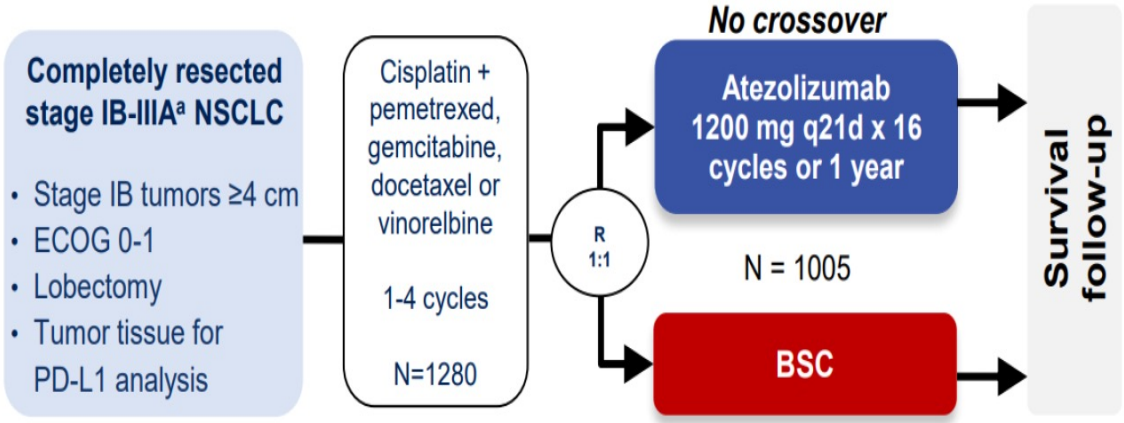
- In PACIFIC, durvalumab started within 42 days of randomization
  - In actual practice even > 42 days
- Molecular alterations, to test or not?
  - Recommend testing and avoid ICI in EGFR/ALK patients
- Treatment duration
  - 1 year

Immunotherapy in Resectable NSCLC

IMpower010: Phase III randomised trial of atezolizumab vs BSC in early-stage NSCLC



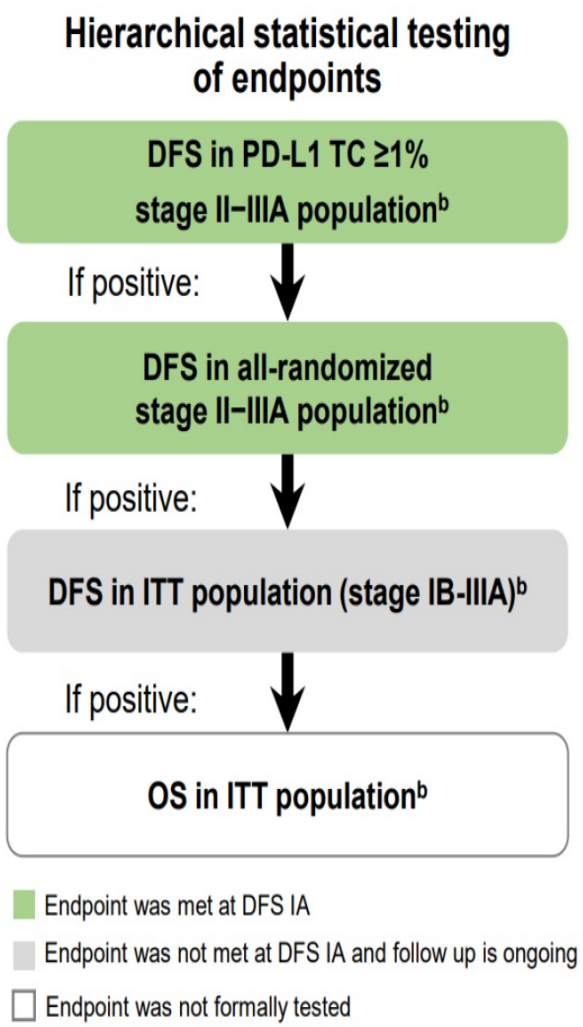
Stratification factors
- Sex | Stage | Histology | PD-L1 status

Primary endpoint
- Investigator-assessed DFS tested hierarchically

Key secondary endpoints
- OS in ITT | DFS in PD-L1 TC ≥50% | 3-yr and 5-year DFS

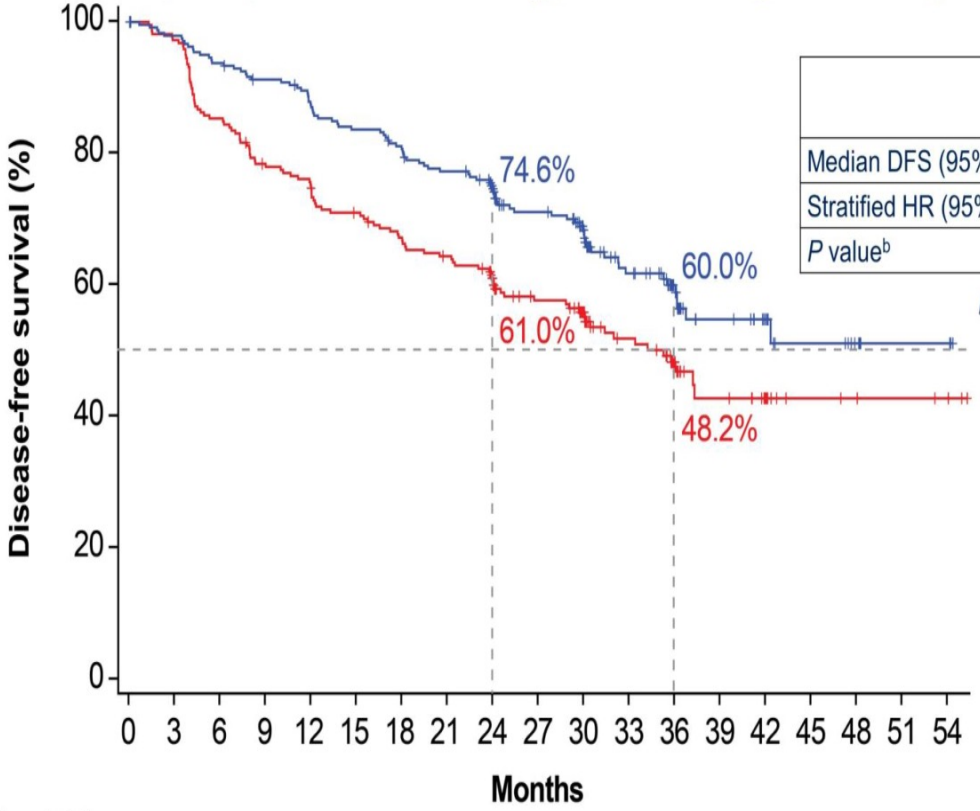
Key exploratory endpoints
- OS biomarker analyses

Clinical cutoff: 18 April 2022. Both arms included observation and regular scans for disease recurrence on the same schedule. ECOG, Eastern Cooperative Oncology Group, q21d, every 21 days.
[a] Per UICC/AJCC staging system, 7th edition. [b] Two-sided α=0.05.



Felip E, WCLC 2022

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population (primary endpoint)



	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]	

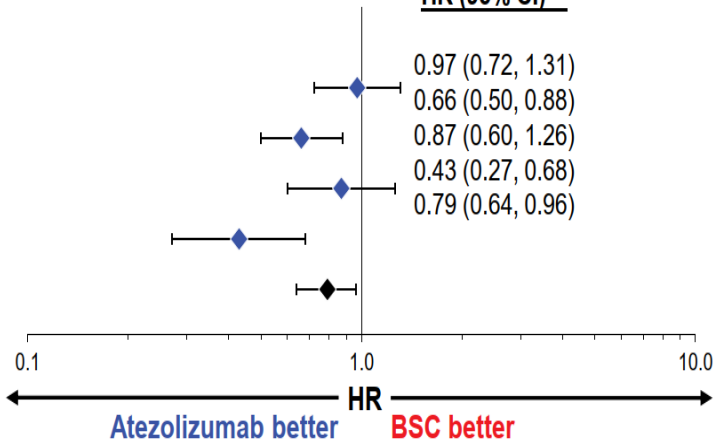
Median follow-up: 32.8 mo (range, 0.1-57.5)

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.

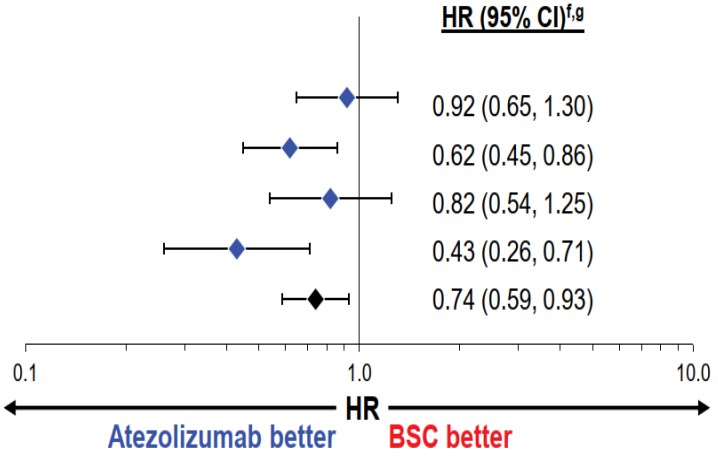
DFS by PD-L1 status[a]

All-randomised stage II-IIIA population (with and without known EGFR/ALK+ disease)

Subgroup *(including EGFR/ALK+)*	n	HR (95% CI)[b,c]
PD-L1 status by SP263		
TC <1%	383	0.97 (0.72, 1.31)
TC ≥1%	476	0.66 (0.50, 0.88)
TC 1-49%	247	0.87 (0.60, 1.26)
TC ≥50%	229	0.43 (0.27, 0.68)
All patients[d]	882	0.79 (0.64, 0.96)



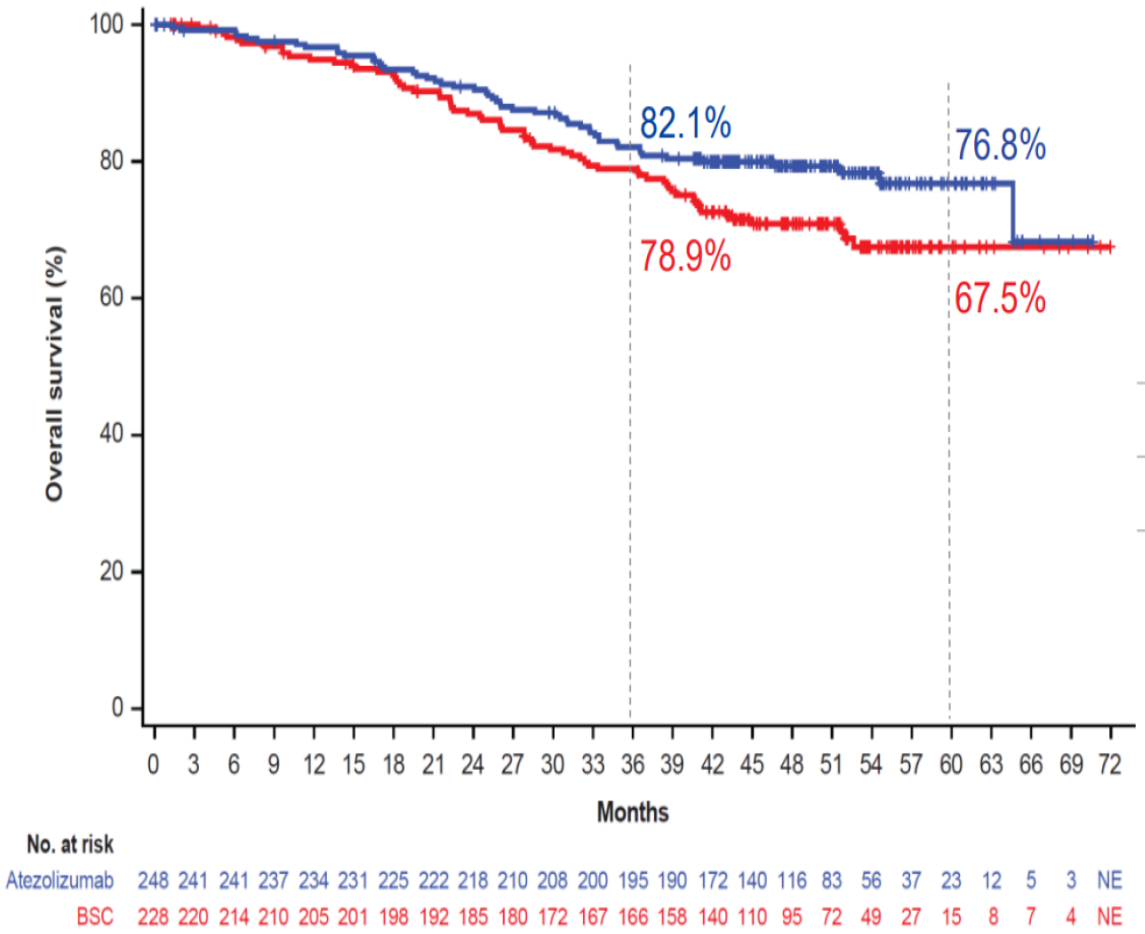
Subgroup *(excluding EGFR/ALK+)*[e]	n	HR (95% CI)[f,g]
PD-L1 status by SP263		
TC <1%	312	0.92 (0.65, 1.30)
TC ≥1%	410	0.62 (0.45, 0.86)
TC 1-49%	201	0.82 (0.54, 1.25)
TC ≥50%	209	0.43 (0.26, 0.71)
All patients[h]	743	0.74 (0.59, 0.93)



Clinical cutoff: 21 January 2021. [a] Per SP263 assay.
[b] Stratified for all patients and PD-L1 TC ≥1%; unstratified for all other subgroups. [c] DFS analyses in the PD-L1 TC <1% and TC 1-49% subgroups were exploratory. [d] 23 patients had unknown PD-L1 status as assessed by SP263. [e] Excluding patients with known *EGFR/ALK+* NSCLC. [f] Unstratified for all subgroups. [g] EGFR/ALK+ exclusion analyses were post hoc. [h] 21 patients had unknown PD-L1 status as assessed by SP263.

Results of OS IA: PD-L1 TC ≥1%[a] (stage II-IIIA)

(data cutoff: 18 Apr '22, median follow-up: 46 months)



	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[b]	0.71 (0.49, 1.03)	

mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

Immunotherapy in resectable NSCLC

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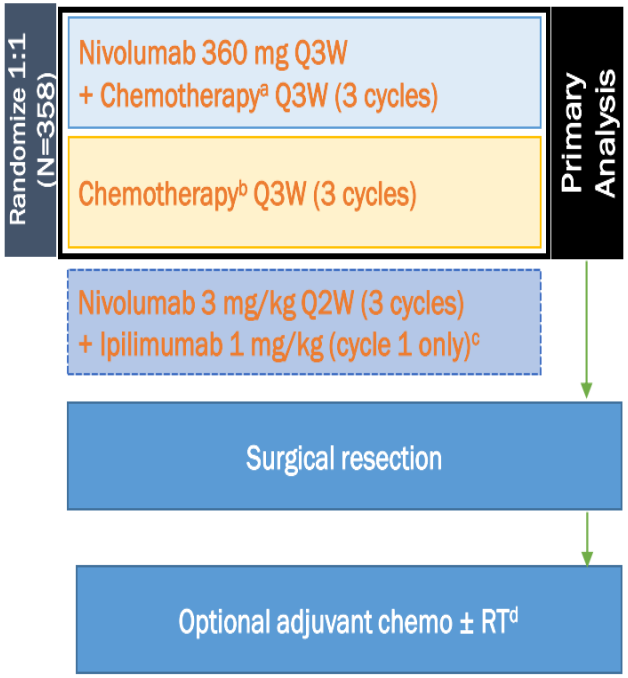
- Neoadjuvant vs Adjuvant (vs Peri-operative)
- Pros
  - Improved tolerability
  - Down staging (greater neoantigen load)
  - Early treatment of micrometastatic disease
- Cons
  - Delay or Eliminate Surgery
  - Risk of post-surgical complications
  - Immune related AEs

Neoadjuvant Nivolumab +CT in Resectable Stage IB-IIIA (CheckMate 816): Study Design and Patients

Key eligibility criteria

- Newly diagnosed, resectable, untreated, unselected, stage IB-IIIA, patients with NSCLC
- No known sensitizing *EGFR* mutations or *ALK* alterations



Patient Characteristics, %		Nivo + chemo (n=179)	Chemo (n=179)
Median age (range), years		64 (41-82)	65 (34-84)
Female, %		28	29
Region[e], n (%)	North America	23	28
	Europe	23	14
	Asia	48	51
Clinical stage[f], n (%)	IB-II[g]	36	35
	IIIA	63	64
Histology, %	Squamous	49	53
	Non-squamous	51	47
Smoking status[h], %	Current / former	89	88
	Never	11	11
Tumor PD-L1 expression, %[i]	Not evaluable	7	7
	<1%	44	43
	≥1%	50	50
	1-49%	28	16
	≥50%	21	24
TMB, %[j]	Not evaluable / not reported	51	50
	<12.3 mut/Mb	27	30
	≥12.3 mut/Mb	22	21

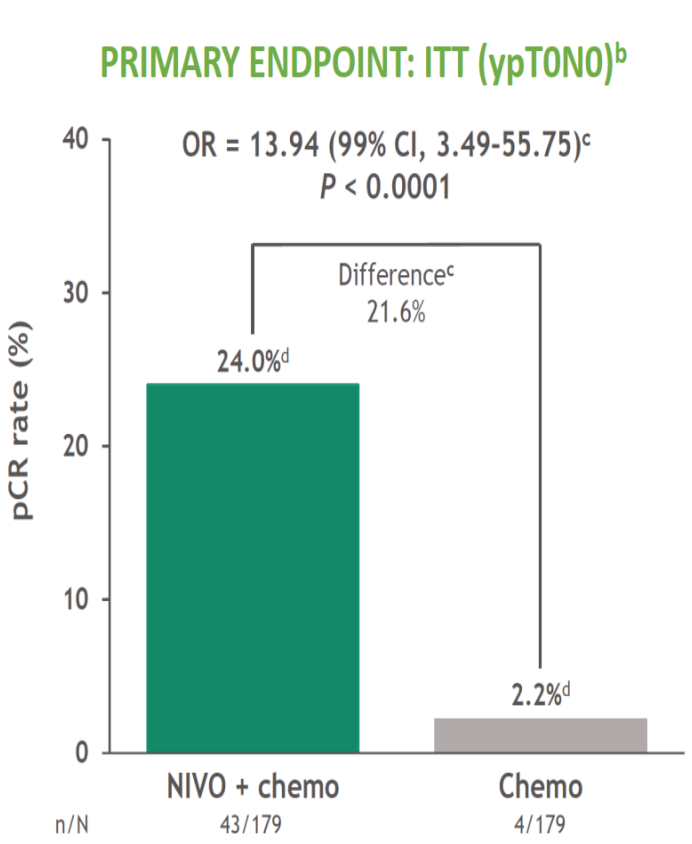
Primary endpoints: pCR by BIPR, EFS by BICR
Secondary endpoints: MPR by BIPR, OS, time to death or distant metastases
Exploratory endpoints: ORR by BICR, predictive biomarkers (PD-L1, TMB, ctDNA[k])

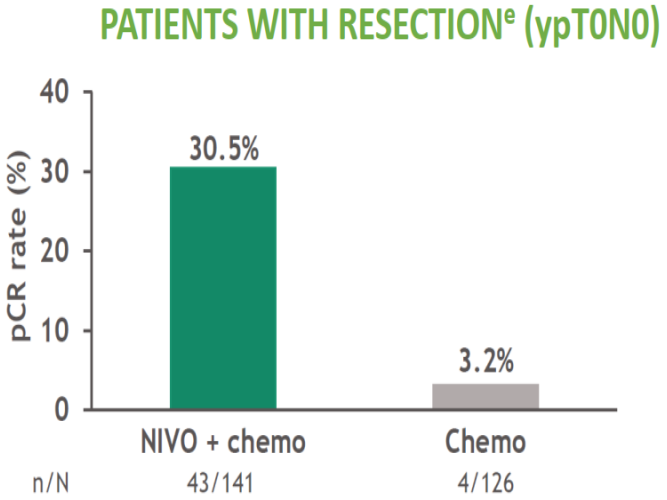
- **Baseline characteristics in the Nivolumab + Ipilimumab (exploratory) arm were generally similar to the NIVO + chemo and chemo arms**

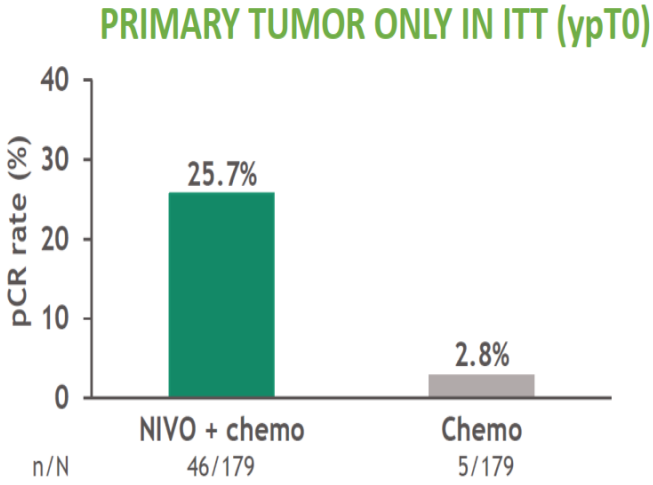
BICR, Blinded Independent Central Review; BIPR, Blinded Independent Pathology Review; EFS, event-free survival, NSCLC, non small cell lung cancer; ORR, overall response rate; pCR, pathological complete response.
[a]NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; [b]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin; [c]Randomized exploratory arm (enrollment closed early); [d]Per healthcare professional choice; [e]Rest of the world: 7% of patients in each of the NIVO + chemo and chemo arms; [f]Disease stage by CRF, with TNM 7 th edition used for classification; 1 patient in each of the NIVO + chemo and chemo arms had stage IV disease; [g]Stage IB, IIA, IIB disease: 6%, 17%, and 14% of patients in the NIVO + chemo arm, and 4%, 18%, and 13% in the chemo arm, respectively; [h]Smoking status unknown: 1 patient in chemo arm; [i]Percentages are based on ITT; [j]TMB was not analyzed for patients in China, and these patients are included in the "not reported" category; [k]Performed using tumor guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring).
1. NCT02998528. 2. Forde P, et al. American Association for Cancer Research Annual Meeting 2021. Presentation CT003.

Forde, AACR 2021

Neoadjuvant Nivolumab + CT in Resectable Stage IB-IIIA (CheckMate 816): pCR[a] Rate





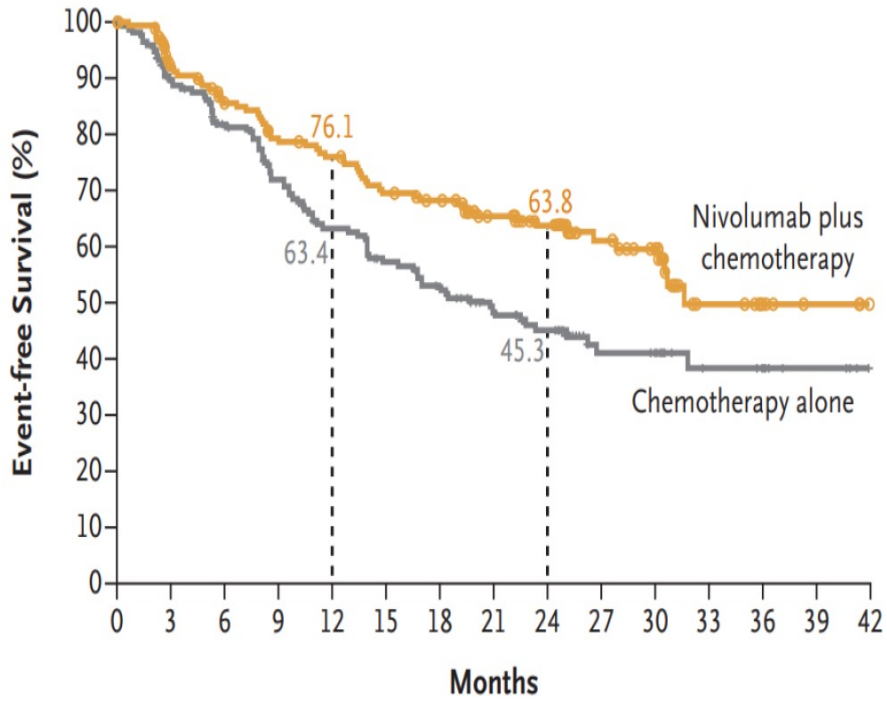


- **pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4 29.0)**

CT, chemotherapy.
[a]Per BIPR; pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]ITT principle: patients who did not undergo surgery counted as non responders for primary analysis; [c]Calculated by stratified Cochran Mantel Haenszel method; [d]pCR rates 95% CI: NIVO + chemo, 18.0 31.0; chemo, 0.6 5.6; [e]Patients who underwent definitive surgery with an evaluable pathology sample for BIPR.
Forde P, et al. American Association for Cancer Research Annual Meeting 2021. Presentation CT003.

Checkmate 816 results

A



	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

No. at Risk

Nivolumab plus chemotherapy	179	151	136	124	118	107	102	87	74	41	34	13	6	3	0
Chemotherapy alone	179	144	126	109	94	83	75	61	52	26	24	13	11	4	0

Neoadjuvant Nivolumab + CT in Resectable Stage IB-IIIA (CheckMate 816): pCR Subgroup Analysis

	pCR[a] rate, %		Unweighted pCR difference, % (95% CI)	Unweighted pCR difference, %
	NIVO + chemo (n = 179)	Chemo (n = 179)		
Overall (N = 358)	24	2		22
< 65 years (n = 176)	27	0		27
≥ 65 years (n = 182)	21	4		17
Male (n = 255)	23	2		20
Female (n = 103)	28	2		26
North America (n = 91)	22	2		20
Europe (n = 66)	24	0		24
Asia (n = 177)	28	3		25
Stage IB-II (n = 128)	**26**	**5**		**21**
Stage IIIA (n = 228)	**23**	**1**		**22**
Squamous (n = 182)	**25**	**4**		**21**
Non-squamous (n = 176)	**23**	**0**		**23**
Current/former smoker (n = 318)	26	2		23
Never smoker (n = 39)	10	0		10
PD-L1 < 1% (n = 155)	**17**	**3**		**14**
PD-L1 ≥ 1% (n = 178)	**33**	**2**		**30**
PD-L1 1-49% (n = 98)	24	0		24
PD-L1 ≥ 50% (n = 80)	45	5		40
TMB < 12.3 mut/Mb (n = 102)	22	2		21
TMB ≥ 12.3 mut/Mb (n = 76)	31	3		28
Cisplatin (n = 258)	22	2		20
Carboplatin (n = 72)	31	0		31

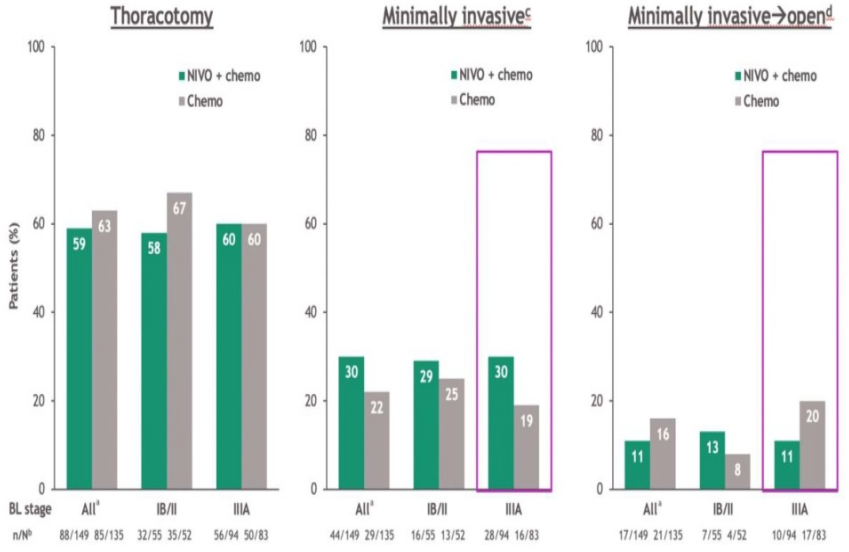
Per BIPR in ITT.

BIPR, Blinded Independent Pathology Review; CT, chemotherapy; ITT, intention-to-treat; TMB, tumor mutation burden.

[a]Per BIPR; MPR: ≤ 10% residual viable tumor cells in both the primary tumor (lung) and sampled lymph nodes; [b]Calculated by stratified Cochran Mantel Haenszel method; [c]MPR rates 95% CI: NIVO + chemo, 29.8 44.4; chemo, 5.2 14.1; [d]Patients who underwent definitive surgery with an evaluable pathology sample for BIPR.

Forde P, et al. American Association for Cancer Research Annual Meeting 2021. Presentation CT003.

Surgical approach by baseline stage of disease

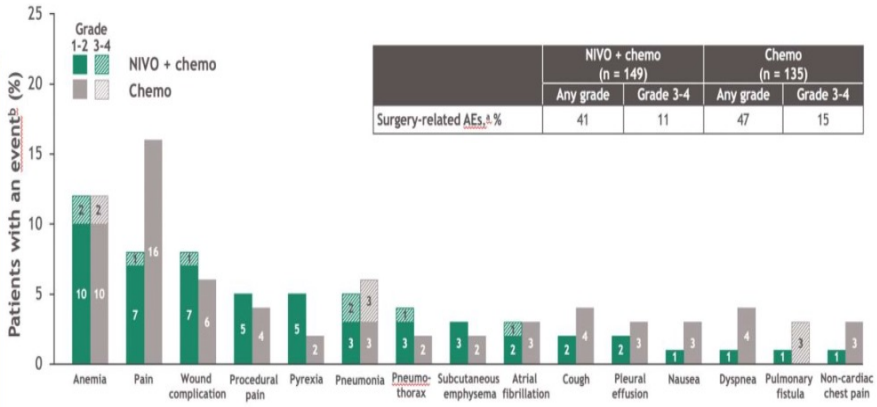


Nivo + chemo resulted in more minimally invasive surgeries and fewer pneumonectomies

Nivo+ chemo did not increase surgery related AEs

Jonathan Spicer, abstract 8503

90-Day surgery-related complications summary[a]



	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

Quo Vadis?

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Is it Adjuvant or Neoadjuvant or Perioperative

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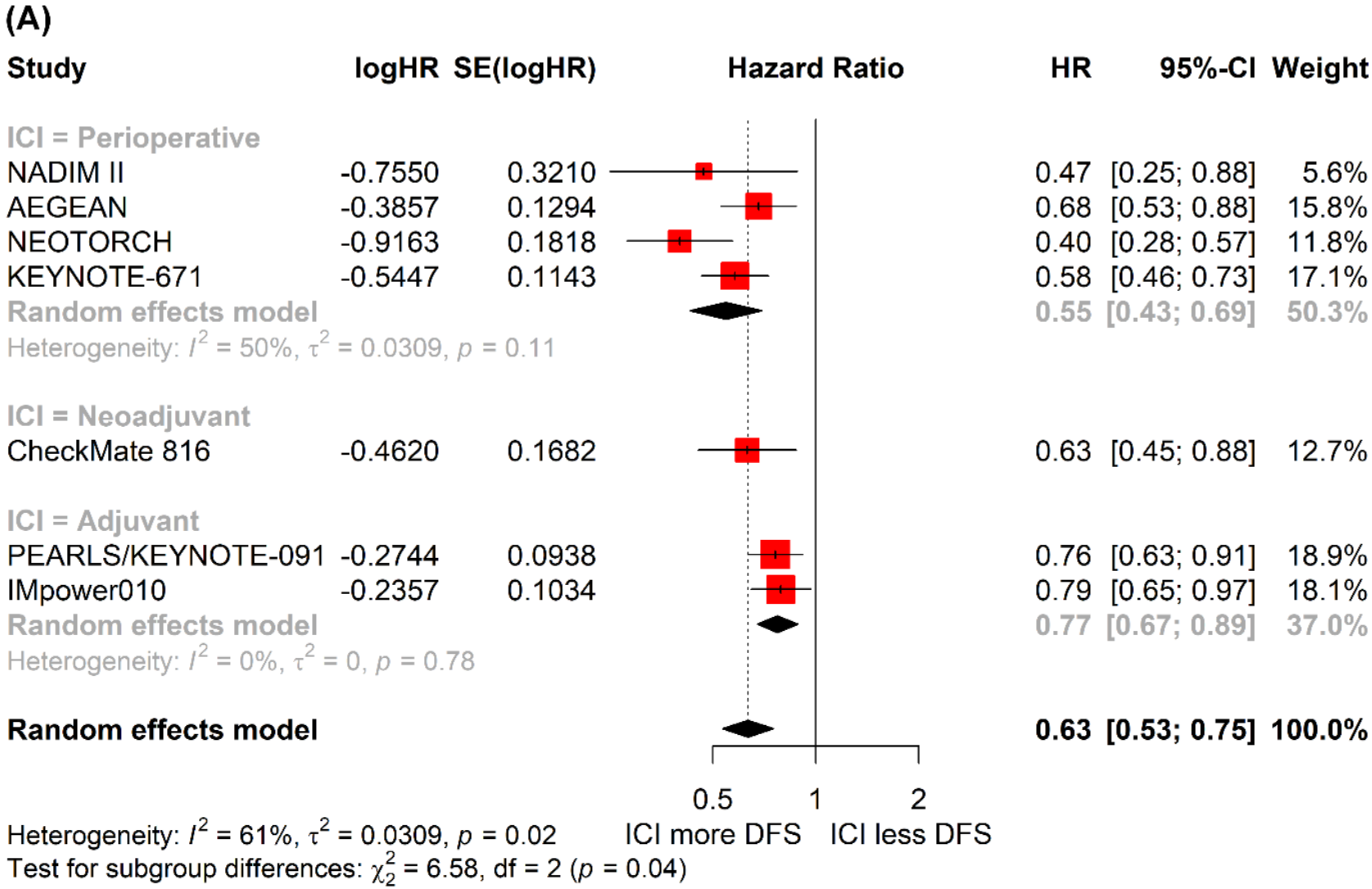

Is it Adjuvant or Neoadjuvant or Perioperative

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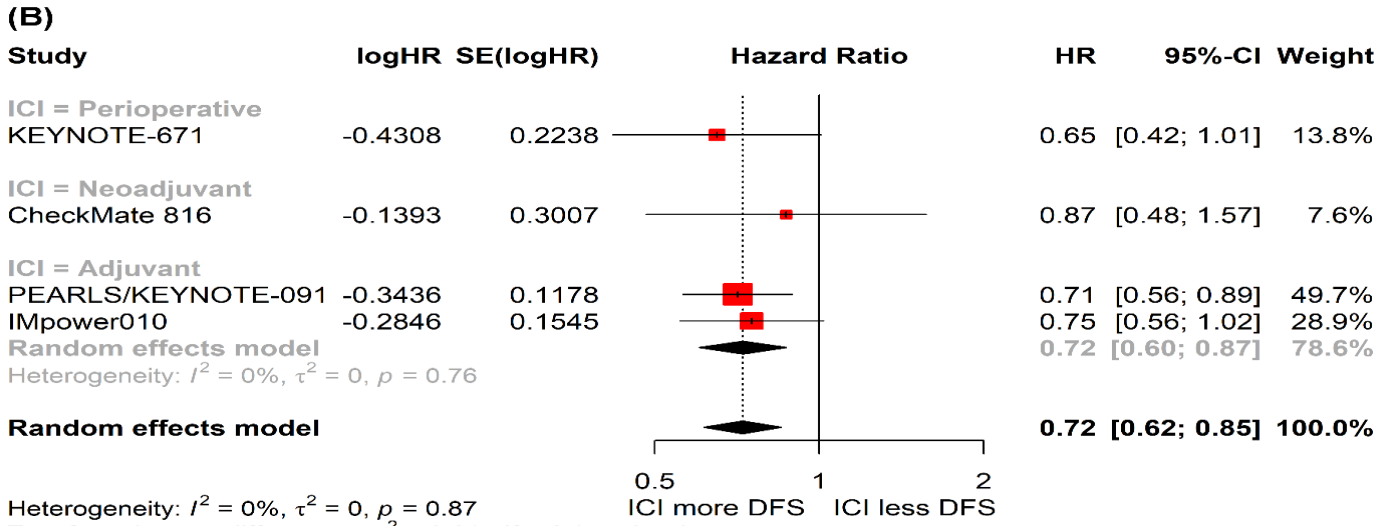
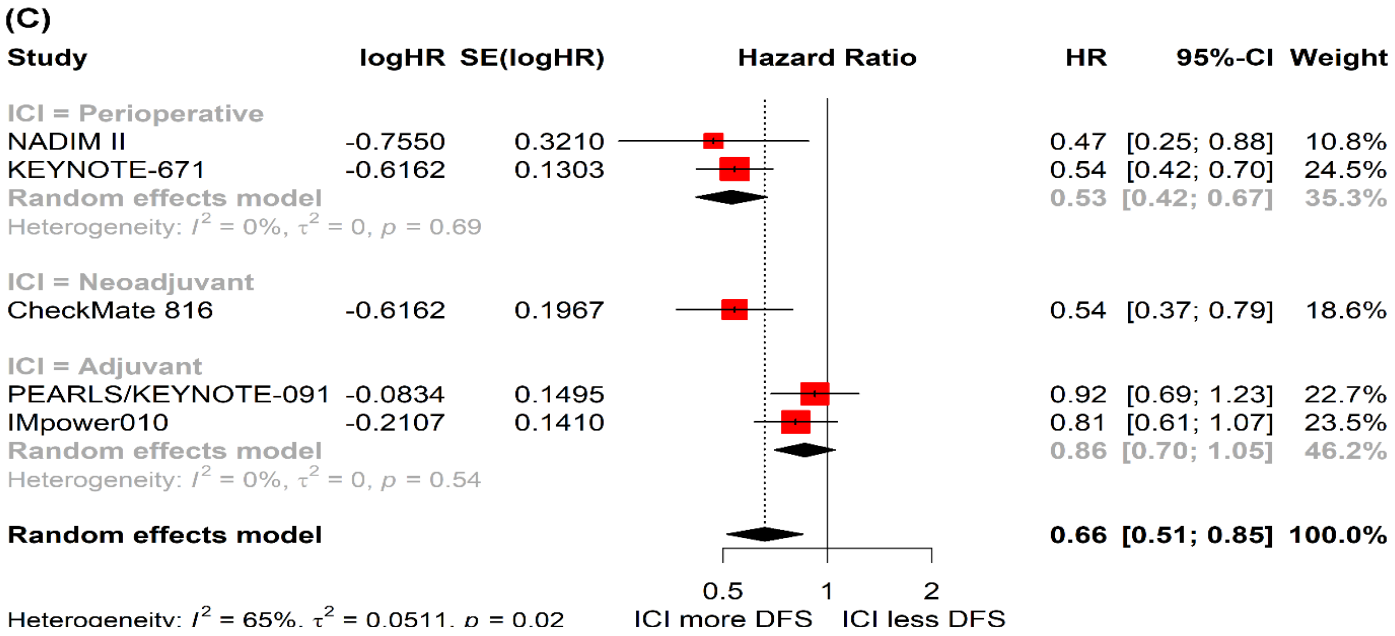
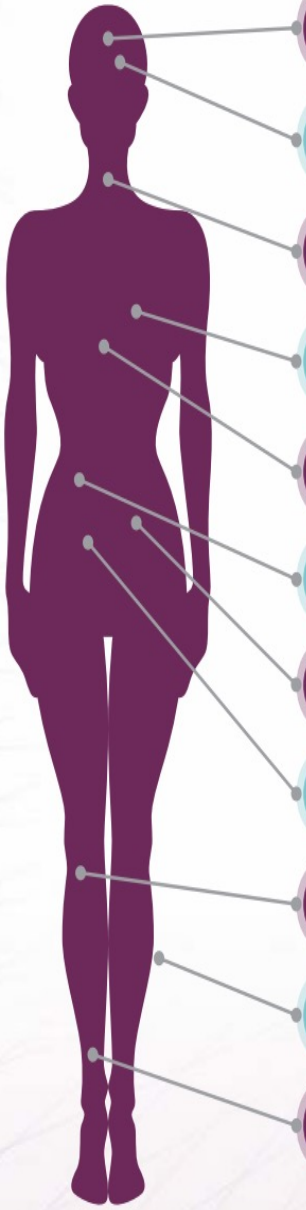




- Limited data due to early release
- In stages I & II DFS benefit appears to be similar for adj vs Neo adj vs periop
- In stage III NeoAdj/Periop better than adjuvant for DFS?

Safety

Spectrum of toxicity of PD-L1/PD-1 inhibitors

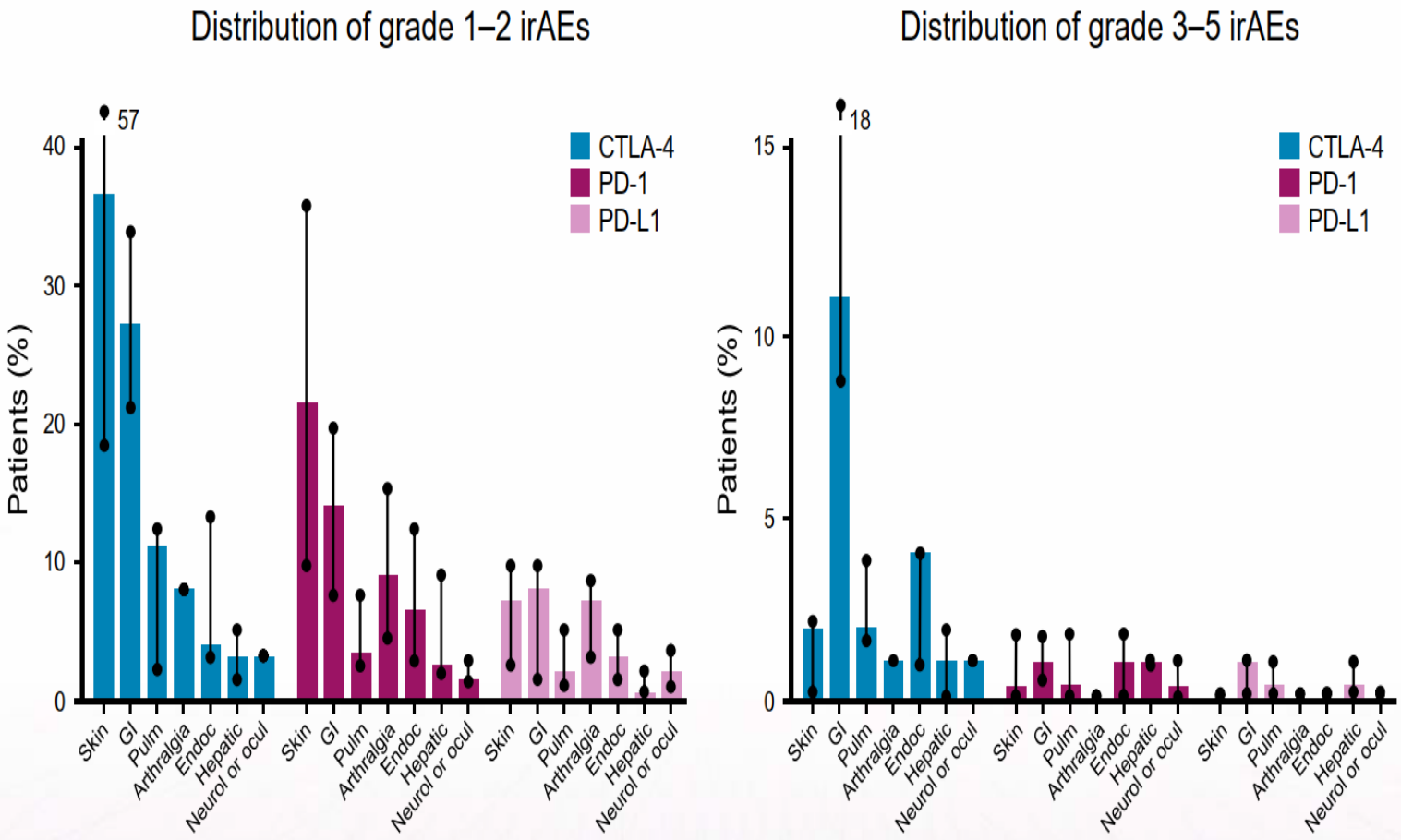


Neurological	Neuropathy • Guillain-Barré • Myelopathy • Meningitis • Encephalitis • Myasthenia
Eye	(Epi)scleritis • Uveitis • Conjunctivitis • Blepharitis • Retinitis
Endocrine	Hyper-/hypothyroidism • Hypophysitis • Diabetes • Adrenal insufficiency
Respiratory	Pneumonitis • Pleuritis • Sarcoid-like granulomatosis
Cardiovascular	Vasculitis • Myocarditis • Pericarditis
Liver	Hepatitis
Renal	Nephritis
Gastrointestinal	Colitis • Ileitis • Pancreatitis • Gastritis
Musculoskeletal	Arthritis • Dermatomyositis
Skin	Pruritus • DRESS • Vitiligo • Rash • Psoriasis • Stevens Johnson
Blood	Haemolytic anaemia • Thrombocytopenia • Neutropenia • Haemophilia

Champiat S, et al. Ann Oncol 2016

CONNECT

Distribution of irAEs across tumour types from key trials of single-agent immune checkpoint inhibitors



AEs, adverse events; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; endoc, endocrine; GI, gastrointestinal; irAEs, immune-related adverse events; neurol, neurology; ocul, ocular; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand-1; pulm, pulmonary
Values are median (range) across all trials
Brahmer, et al. J Clin Oncol 2018

CONNECT

Conclusion

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- IO single agent or in combination with chemotherapy is the standard 1st line treatment of non-oncogene addicted NSCLC.
- Role of IO & IO combination is evolving
  - KRAS with STK11 or KEAP1 commutated
  - Patients with good PS and not receiving chemotherapy
- Durvalumab consolidation is now standard of care after CRT for stage III non-EGFR/ALK NSCLC
- More systemic treatment options for patients with resectable NSCLC
  - Adjuvant vs Neoadjuvant vs Perioperative
- Neoadjuvant offers some unique advantages but is subsequent adjuvant IO needed? Who needs perioperative IO?
- Biomarkers development might help select patients appropriate for the different treatment options.