Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy for the Treatment of Lung Cancer

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

Society for Immunotherapy of Cancer

Disclosures

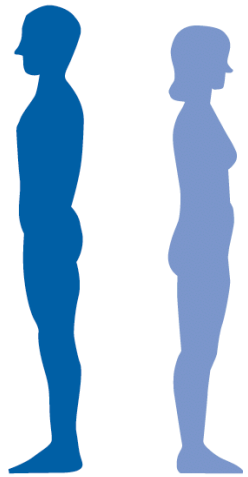
- Contracted Research: AstraZeneca, Bristol Myers Squibb, Novartis, Regeneron, Tesaro, Karyopharm, Debiopharm
- Consulting Fees: Novartis
- I will be discussing non-FDA approved indications during my presentation.

Lung cancer

- 80-85% non-small cell lung cancer (NSCLC)
- 10-15% small-cell lung cancer (SCLC)
- Leading cause of cancer-related mortality in both men and women.

Estimated Deaths

Male			Female		
Lung & bronchus	72,500	23%	Lung & bronchus	63,220	22%
Prostate	33,330	10%	Breast	42,170	15%
Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
Pancreas	24,640	8%	Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%	Ovary	13,940	5%
Leukemia	13,420	4%	Uterine corpus	12,590	4%
Esophagus	13,100	4%	Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%	Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
All sites	**321,160**		**All sites**	**285,360**	



American Cancer Society 2020

FDA-approved checkpoint inhibitors in lung cancer

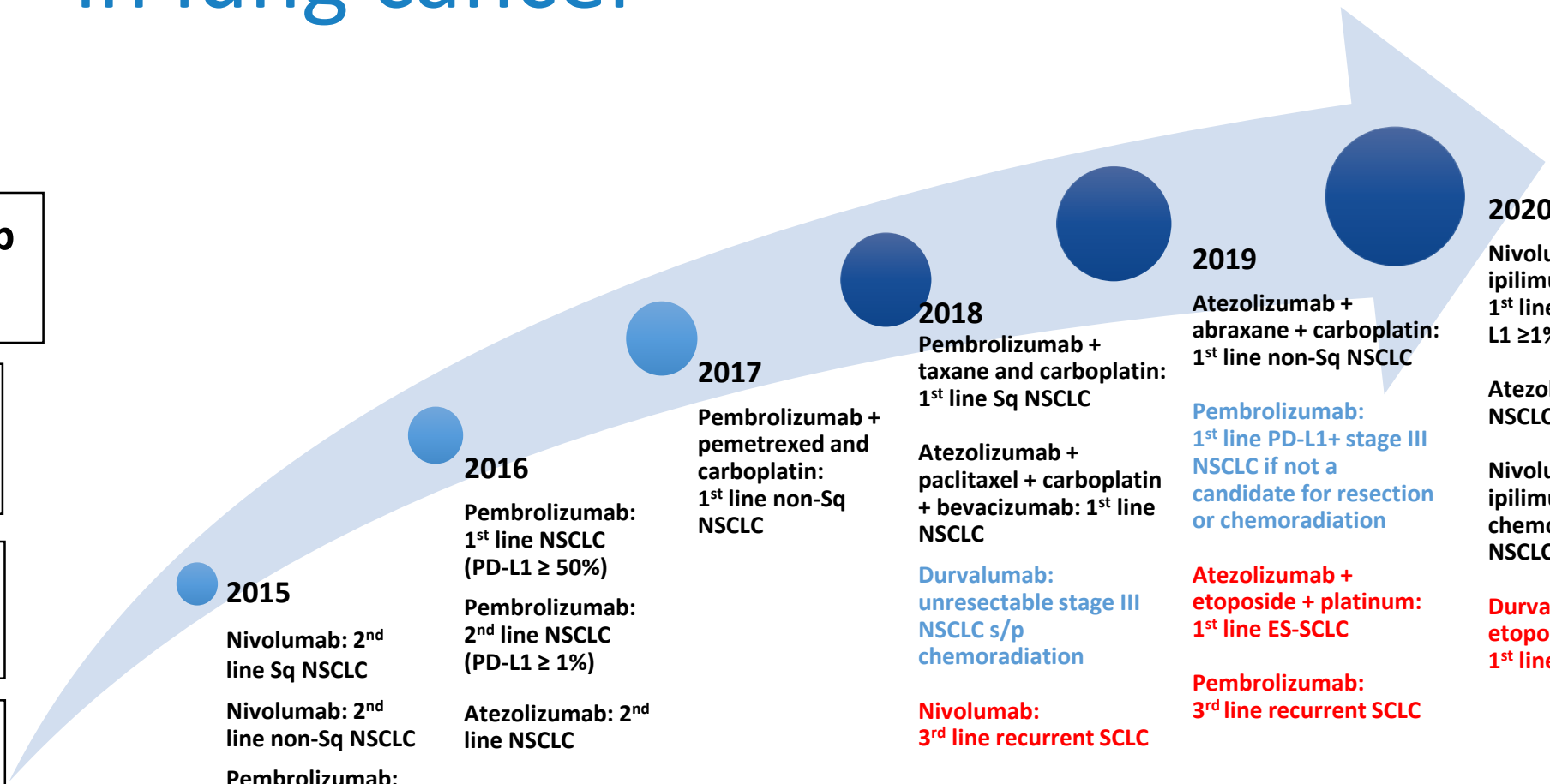
Nivolumab — PD-1

Pembrolizumab — PD-1

Atezolizumab — PD-L1

Durvalumab — PD-L1

Ipilimumab — CTLA-4



2015

Nivolumab: 2nd line Sq NSCLC

Nivolumab: 2nd line non-Sq NSCLC

Pembrolizumab: 2nd line NSCLC (PD-L1 ≥ 50%)

2016

Pembrolizumab: 1st line NSCLC (PD-L1 ≥ 50%)

Pembrolizumab: 2nd line NSCLC (PD-L1 ≥ 1%)

Atezolizumab: 2nd line NSCLC

2017

Pembrolizumab + pemetrexed and carboplatin: 1st line non-Sq NSCLC

2018

Pembrolizumab + taxane and carboplatin: 1st line Sq NSCLC

Atezolizumab + paclitaxel + carboplatin + bevacizumab: 1st line NSCLC

Durvalumab: unresectable stage III NSCLC s/p chemoradiation

Nivolumab: 3rd line recurrent SCLC

2019

Atezolizumab + abraxane + carboplatin: 1st line non-Sq NSCLC

Pembrolizumab: 1st line PD-L1+ stage III NSCLC if not a candidate for resection or chemoradiation

Atezolizumab + etoposide + platinum: 1st line ES-SCLC

Pembrolizumab: 3rd line recurrent SCLC

2020

Nivolumab + ipilimumab: 1st line NSCLC with PD-L1 ≥1%

Atezolizumab: 1st line NSCLC with PD-L1 ≥50%

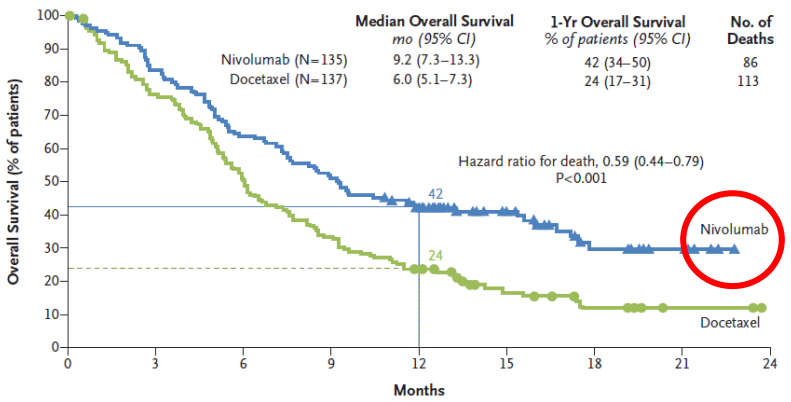
Nivolumab + ipilimumab + chemotherapy: 1st line NSCLC

Durvalumab + etoposide + platinum: 1st line ES-SCLC

Second-line PD-(L)1 blockade improves overall survival in NSCLC

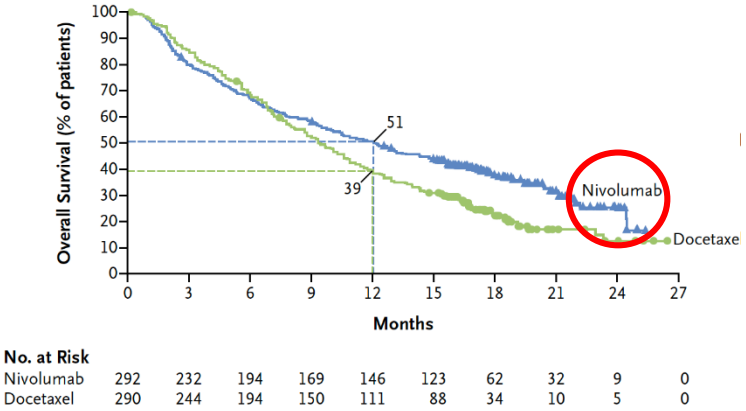
Checkmate-017 (nivolumab 2nd line; squamous NSCLC)

OS



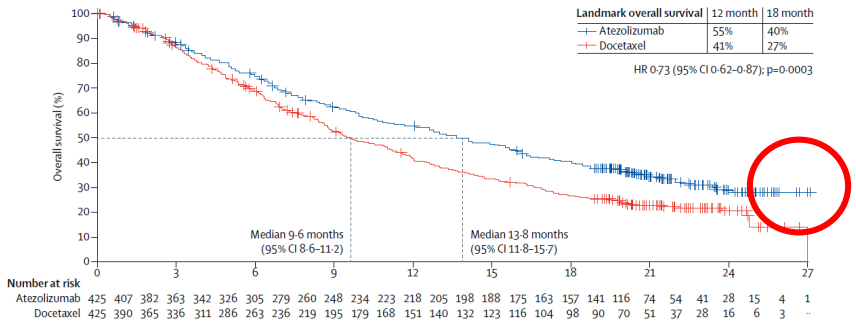
Checkmate-057 (nivolumab 2nd line; non-squamous NSCLC)

OS



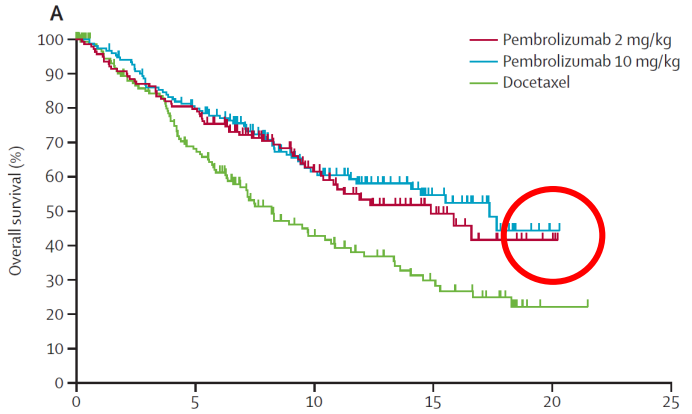
OAK (atezolizumab 2nd line)

OS



Keynote-010 (pembrolizumab 2nd line)

OS



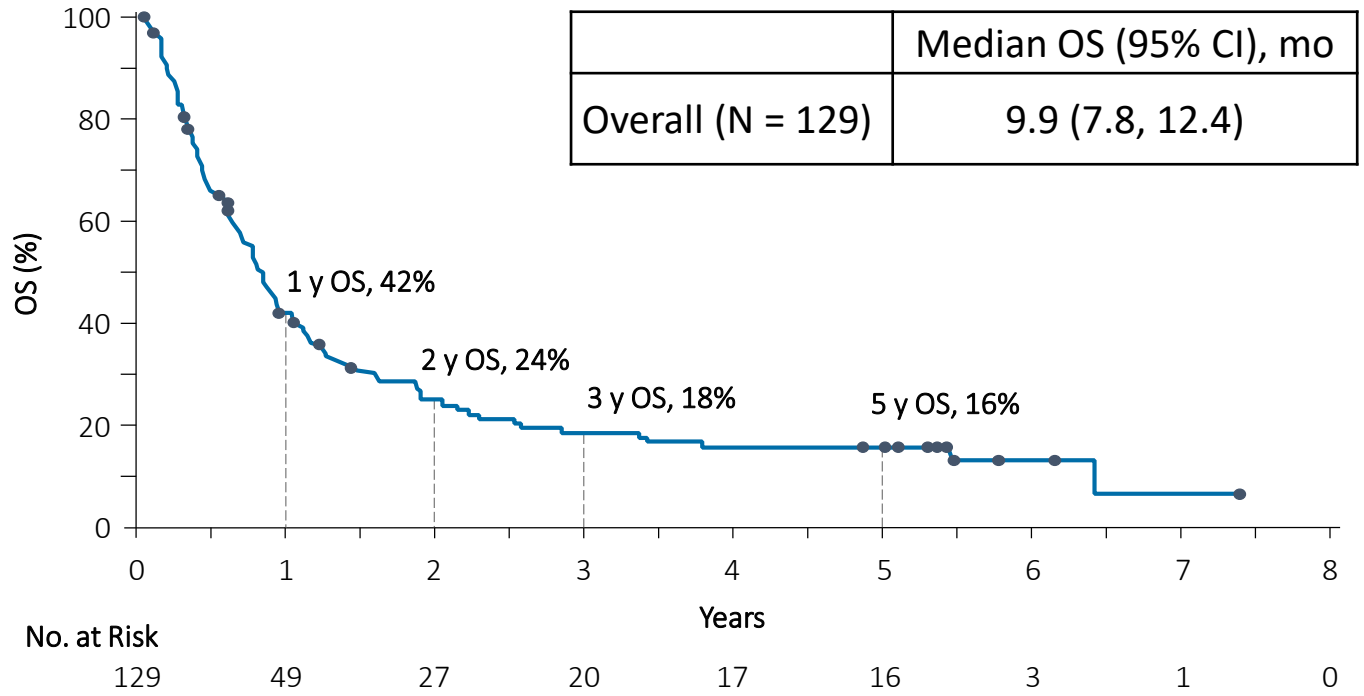
Brahmer et al. NEJM 2015; Borghaei et al. NEJM 2015; Rittmeyer et al. Lancet 2016; Herbst et al. Lancet 2015

CA209-003: Phase 1 study of nivolumab in heavily-treated advanced NSCLC

- First report of long-term survival rate in patients with metastatic NSCLC treated with an immune checkpoint inhibitor.
- According to the National Cancer Institute's SEER data, 5-year survival rate for patients with advanced NSCLC is 4.9%.

5-Year Survival

	Median OS (95% CI), mo
Overall (N = 129)	9.9 (7.8, 12.4)



Gettinger et al., JCO 2018
Brahmer et al., AACR 2017
NCI SEER data, Lung and Bronchus Cancer, 2014

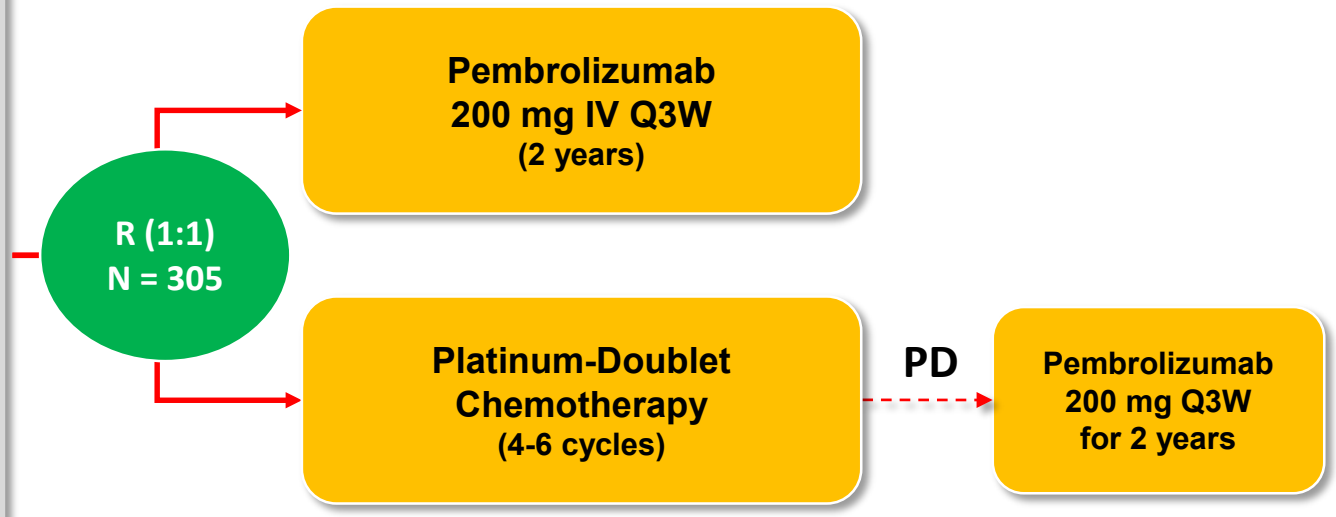
Treatment naïve regimens: competing strategies in metastatic NSCLC

- KEYNOTE-024: Pembrolizumab vs. chemotherapy in PD-L1 at least 50%
- KEYNOTE-042: Pembrolizumab vs. chemotherapy in PD-L1 at least 1%
- KEYNOTE-189: Pembrolizumab plus chemotherapy vs. chemotherapy alone in non-Sq NSCLC
- KEYNOTE-407: Pembrolizumab plus chemotherapy vs. chemotherapy alone in Sq NSCLC
- IMpower 150: Atezolizumab plus chemotherapy/bevacizumab vs. chemotherapy/bevacizumab in non-Sq NSCLC
- IMpower 110: Atezolizumab vs. chemotherapy in PD-L1 at least 1%
- IMpower 130: Atezolizumab plus chemotherapy vs. chemotherapy in non-Sq NCSLC
- CheckMate 227: Nivolumab plus ipilimumab vs. chemotherapy in PD-L1 at least 1%
- CheckMate 9LA: Nivolumab/ipilimumab/chemotherapy (2 cycles) vs. chemotherapy

KEYNOTE-024: Pembrolizumab vs. chemotherapy for PD-L1 ≥ 50% advanced NSCLC

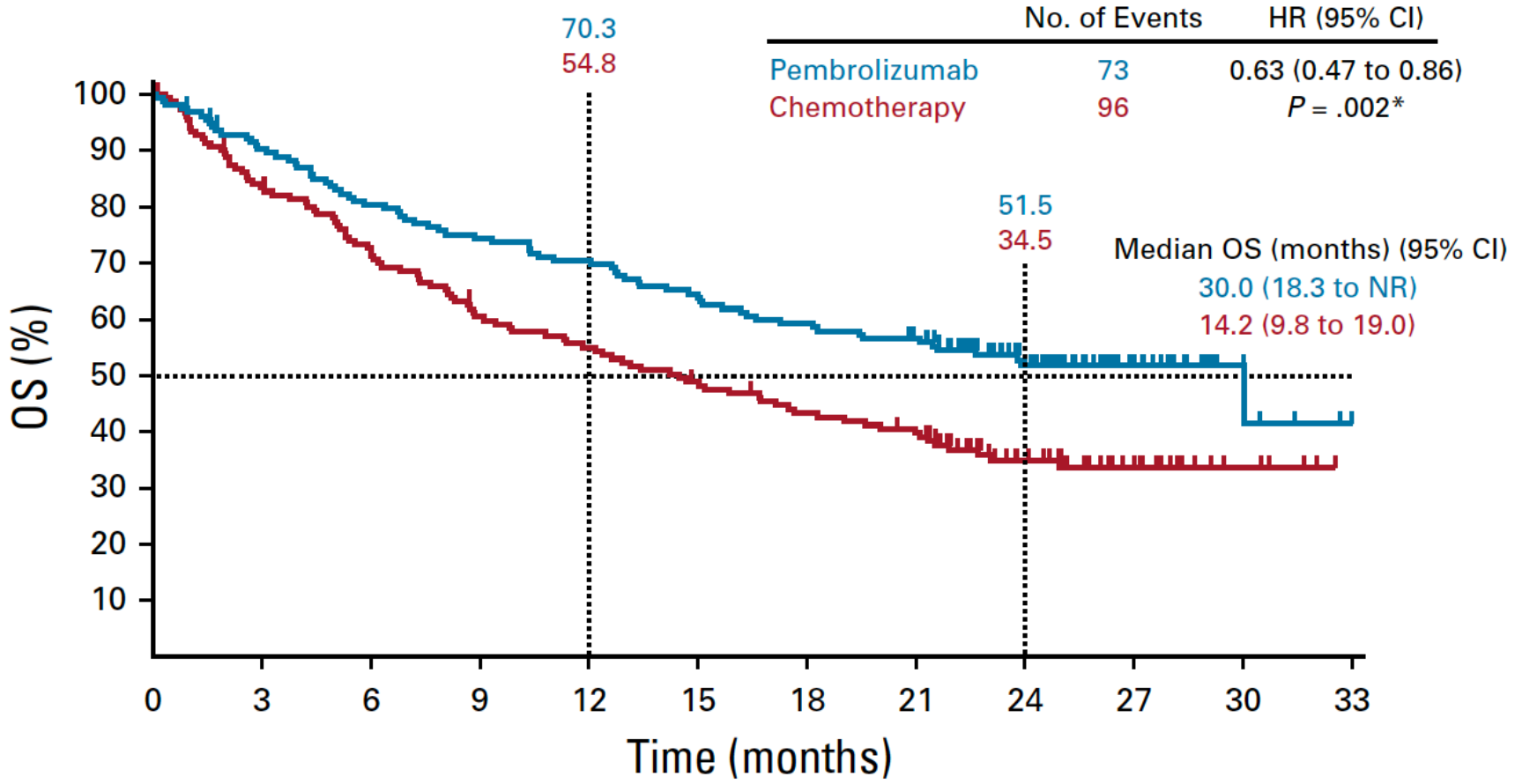
Key Eligibility Criteria

- ***Untreated*** stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No activating *EGFR* mutation or *ALK* translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy



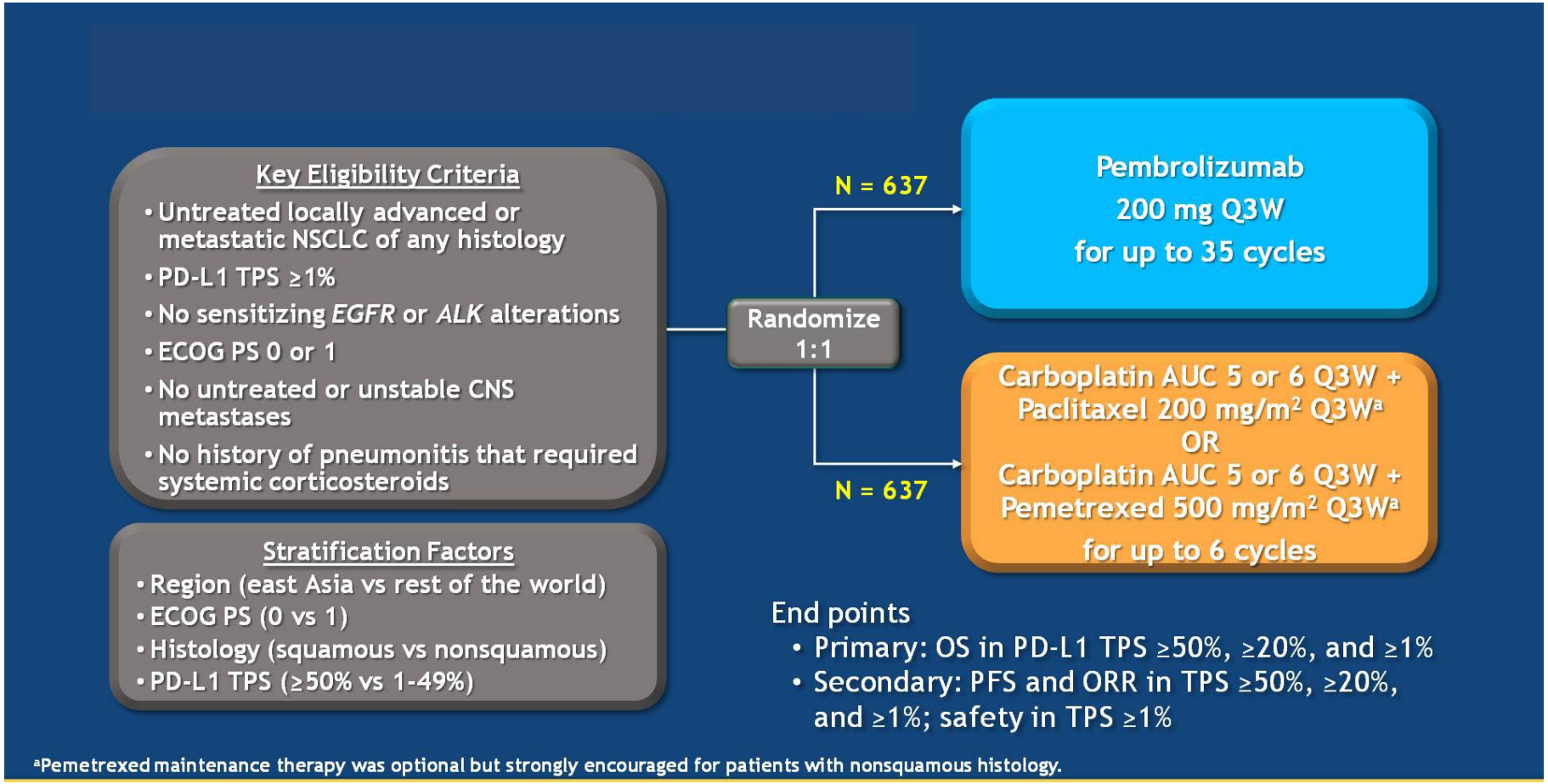
Reck et al., ESMO 2016, NEJM 2016

KEYNOTE-024: Pembrolizumab vs. chemotherapy for PD-L1 ≥ 50% advanced NSCLC



Reck et al., JCO 2019

KEYNOTE-042: Pembrolizumab vs. chemotherapy for PD-L1 ≥ 1% advanced NSCLC



Lopes et al., ASCO 2018

KEYNOTE-042: Pembrolizumab vs. chemotherapy for PD-L1 ≥ 1% advanced NSCLC

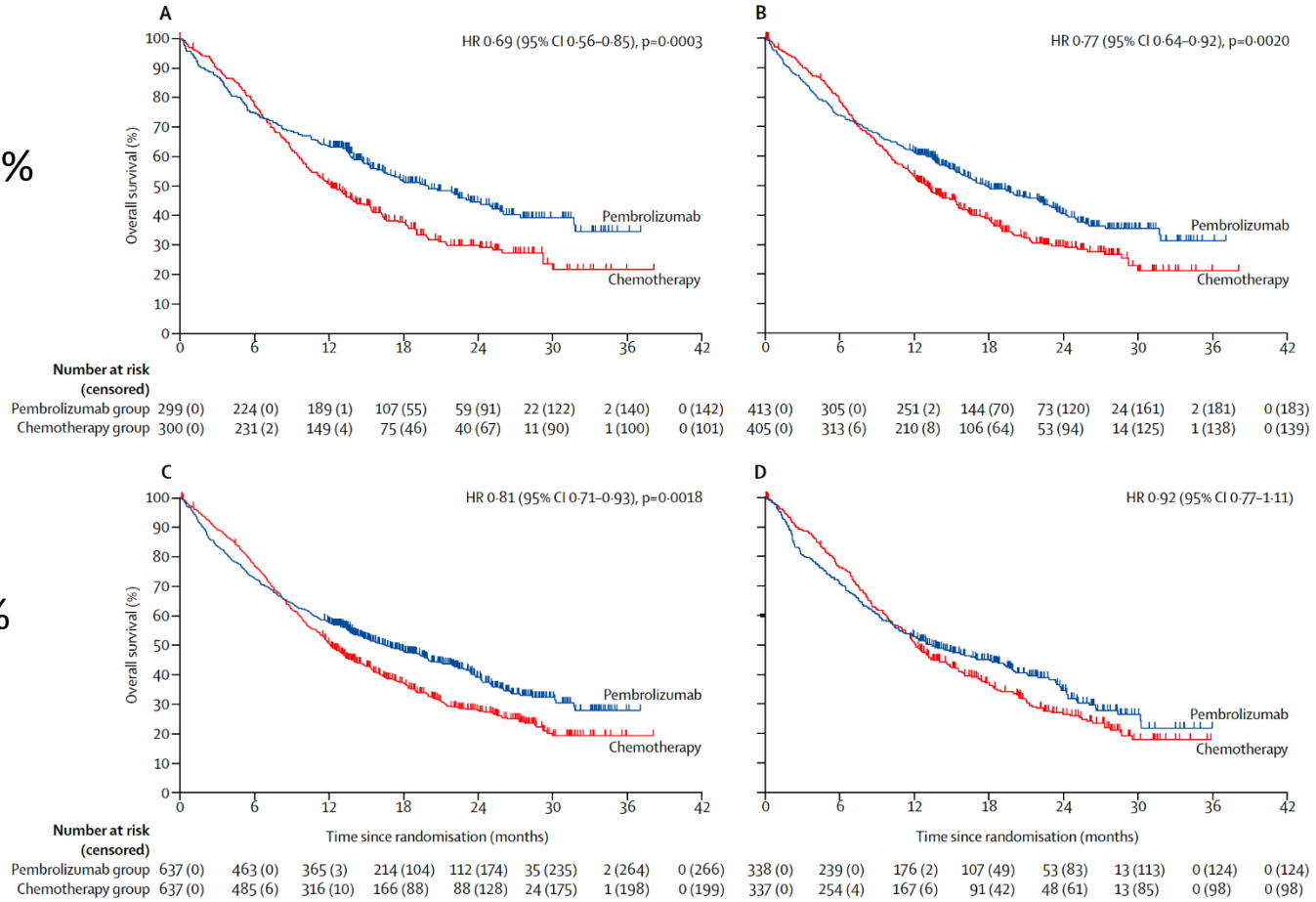
Overall survival

PD-L1 ≥ 50%

PD-L1 ≥ 20%

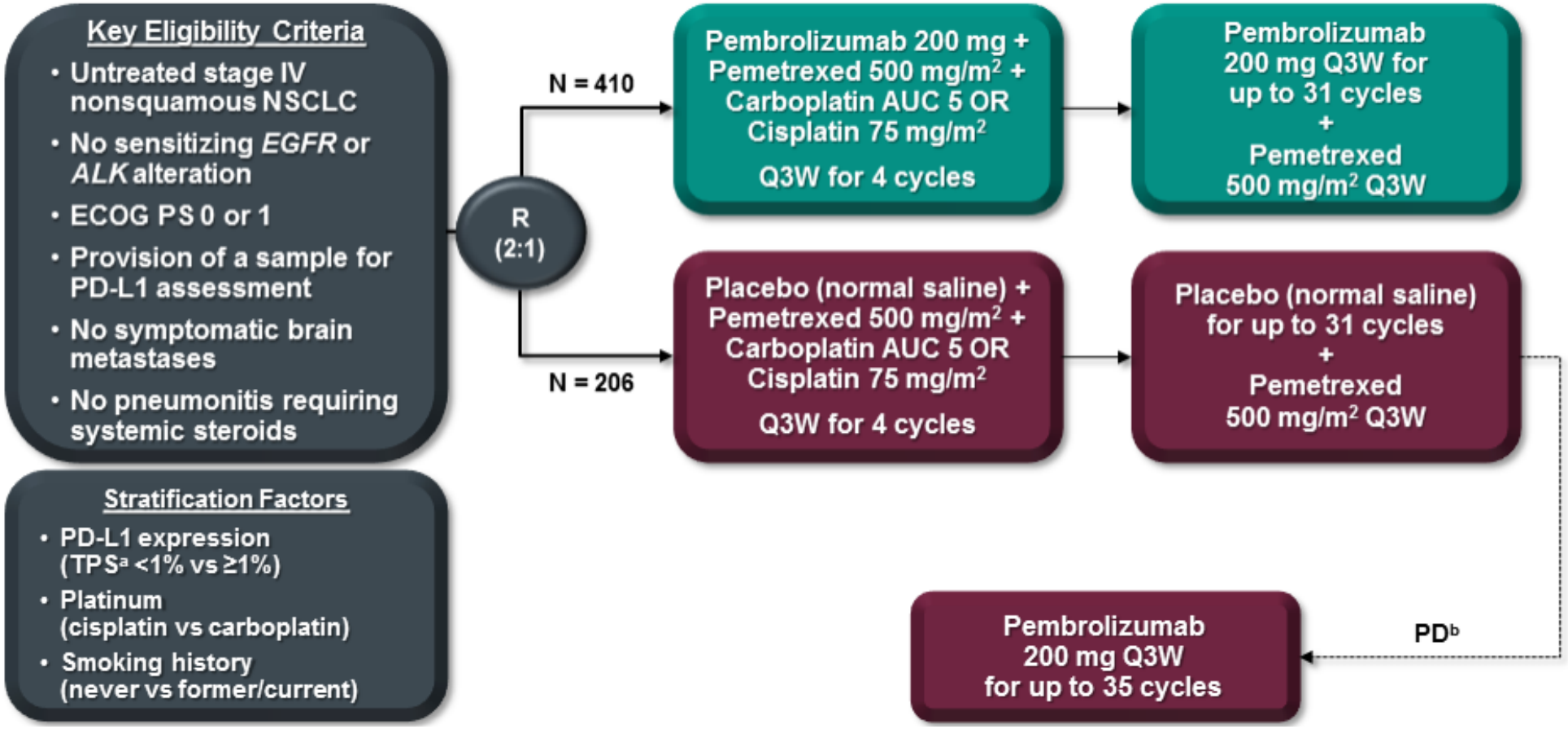
PD-L1 ≥ 1%

PD-L1 1-49%
(exploratory analysis)



Mok et al., Lancet 2019

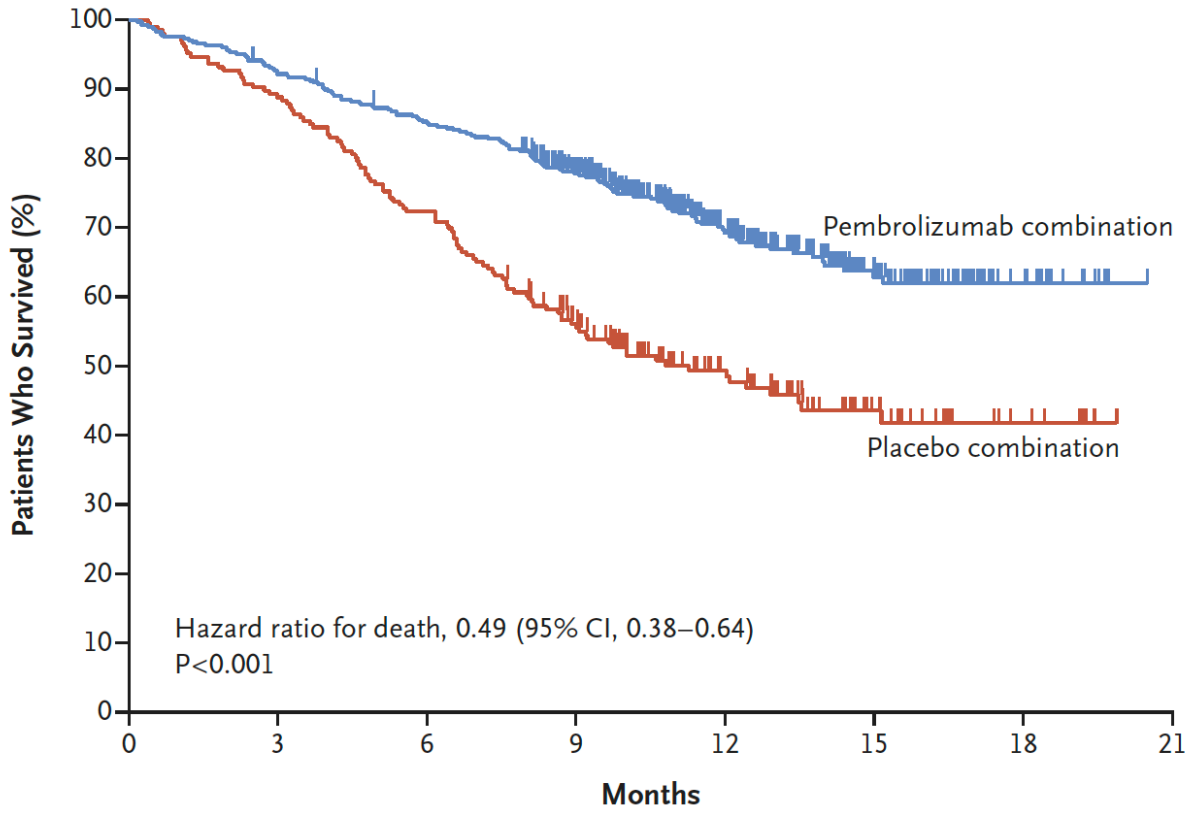
KEYNOTE-189: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced non-squamous NSCLC



Ghandi et al., NEJM 2018

KEYNOTE-189: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced non-squamous NSCLC

Overall survival



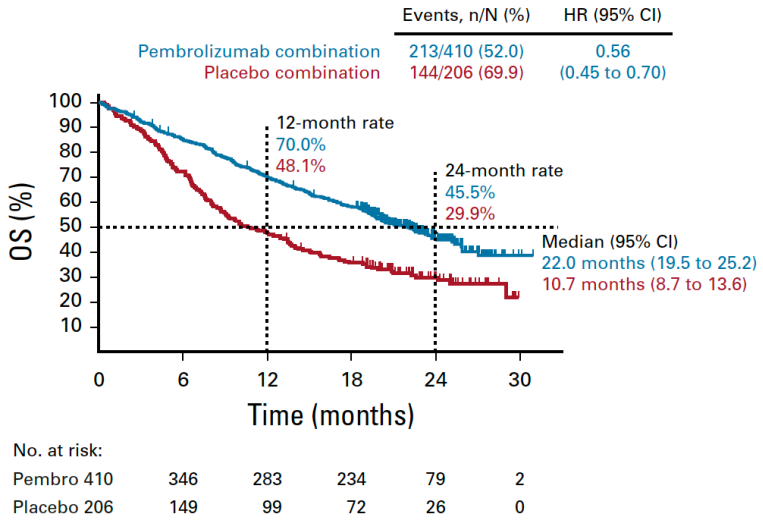
No. at Risk								
Pembrolizumab combination	410	377	347	278	163	71	18	0
Placebo combination	206	183	149	104	59	25	8	0

Ghandi et al., NEJM 2018

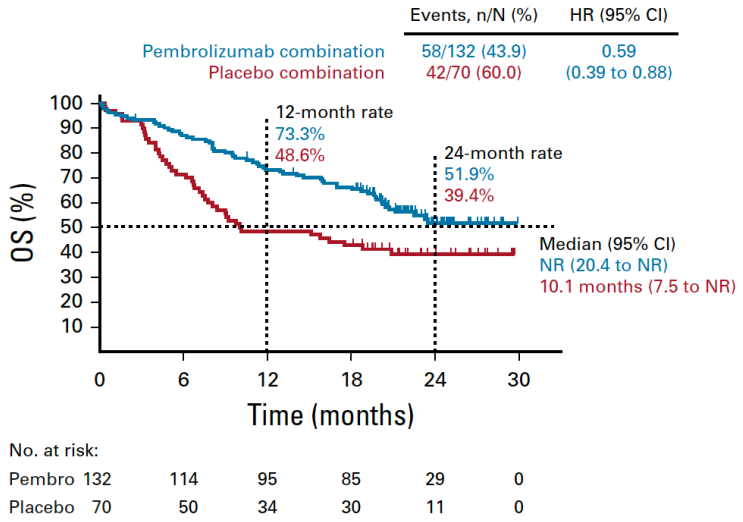
KEYNOTE-189: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced non-squamous NSCLC

Overall survival

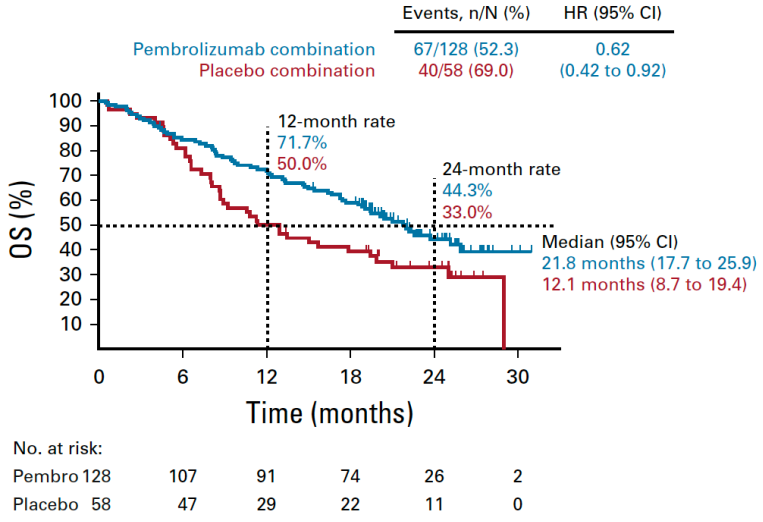
Total population



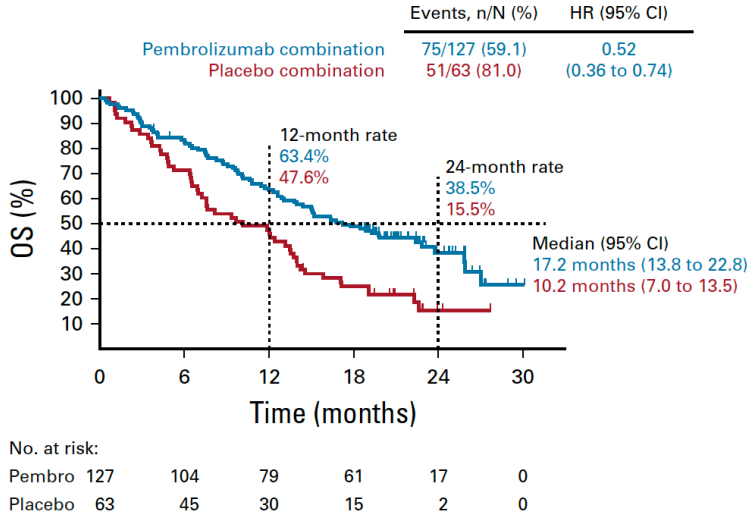
PD-L1 ≥ 50%



PD-L1 1-49%

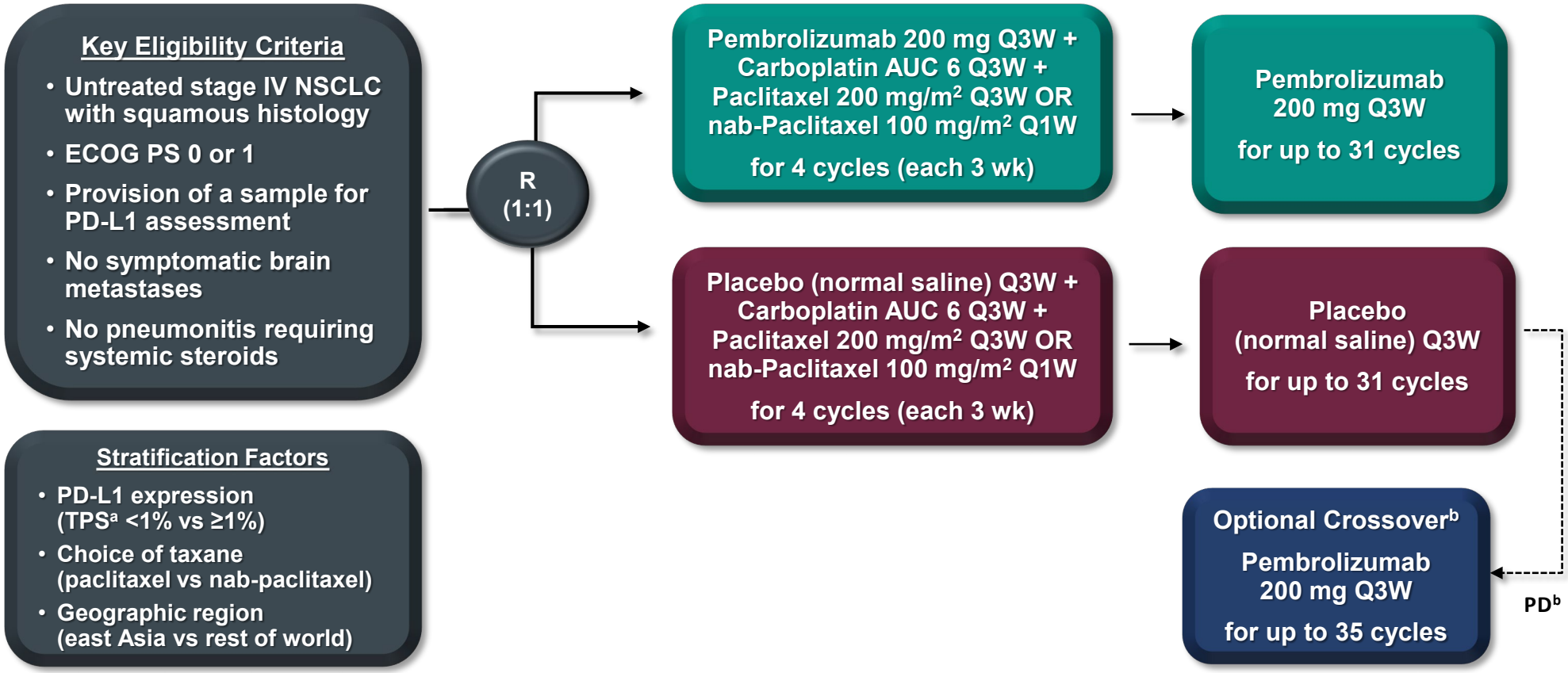


PD-L1 < 1%



Gadgeel et al., JCO 2020

KEYNOTE-407: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced squamous NSCLC

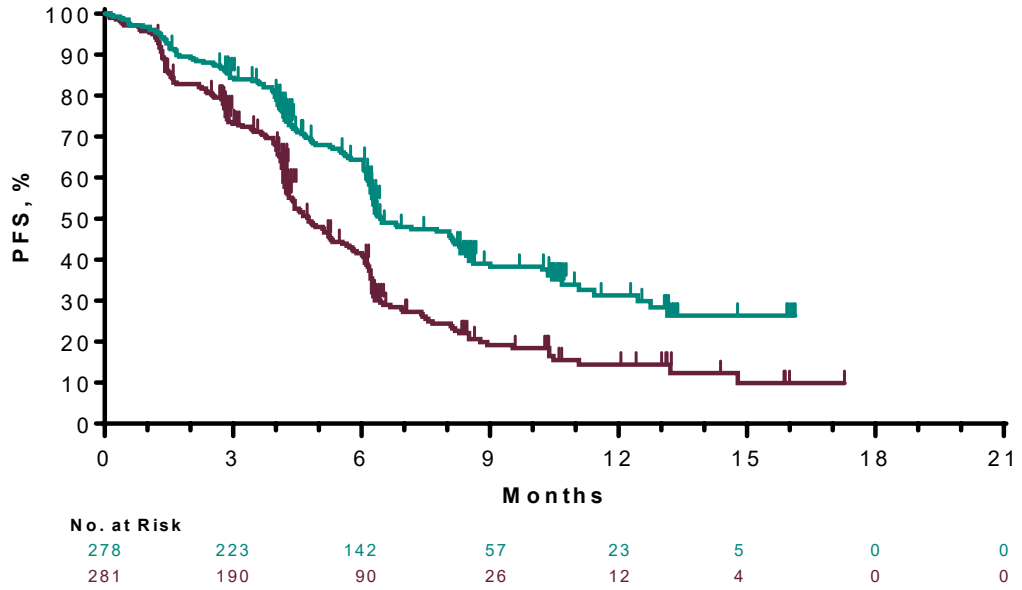


Paz-Ares et al., ASCO 2018

KEYNOTE-407: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced squamous NSCLC

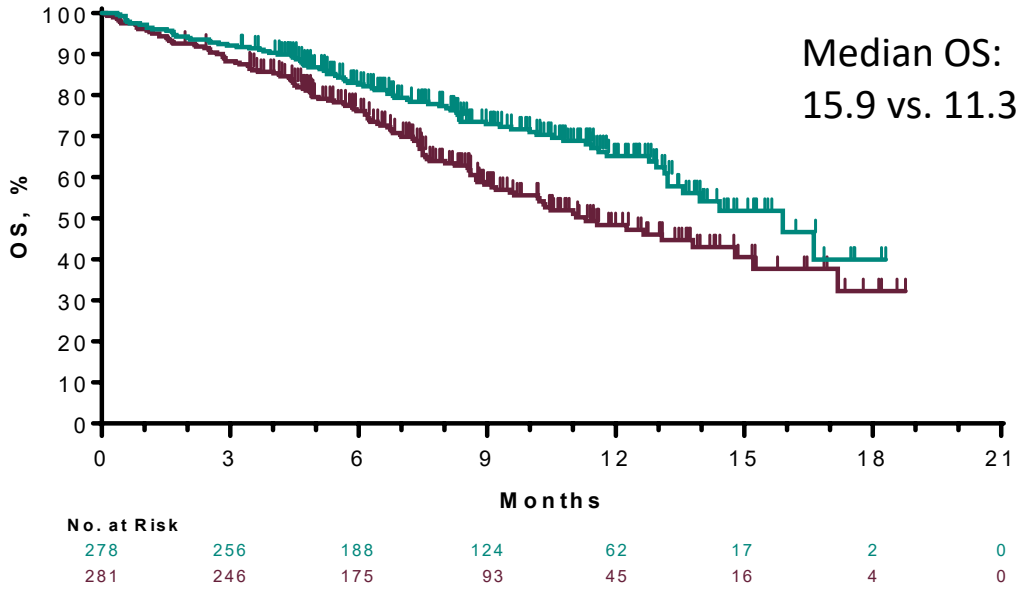
Progression-free survival

	Events	HR (95% CI)	*P*
Pembro + Chemo	54.7%	0.56 (0.45-0.70)	<0.0001
Placebo + Chemo	70.1%		



Overall Survival

	Events	HR (95% CI)	*P*
Pembro + Chemo	30.6%	0.64 (0.49-0.85)	0.0008
Placebo + Chemo	42.7%		



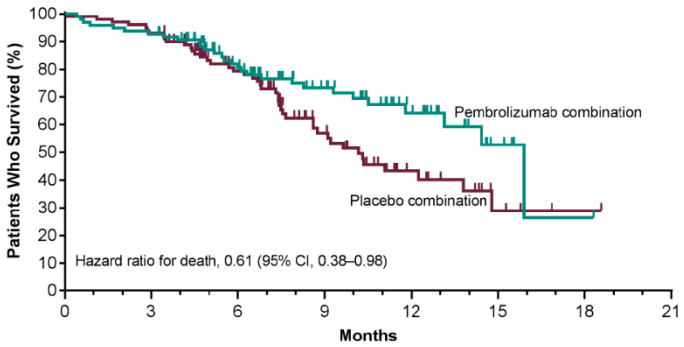
Median OS:
15.9 vs. 11.3 months

Paz-Ares et al., ASCO 2018

KEYNOTE-407: Pembrolizumab plus chemotherapy vs. chemotherapy for advanced squamous NSCLC

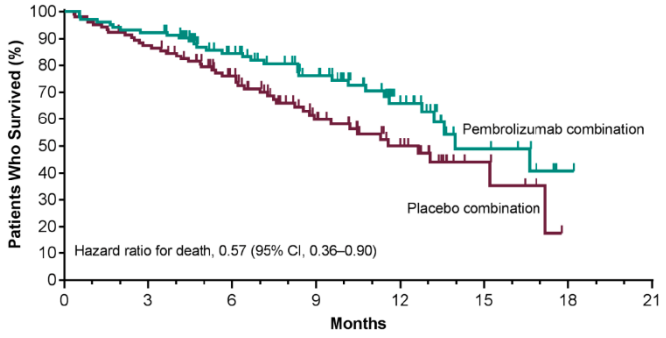
Overall survival

PD-L1 < 1%



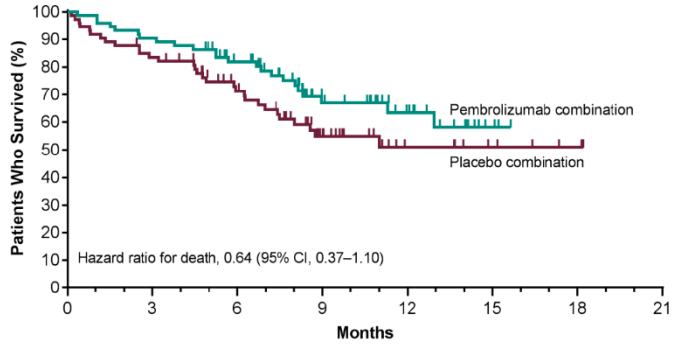
No. at Risk								
Pembrolizumab combination	95	88	62	41	20	5	1	0
Placebo combination	99	92	63	32	14	4	1	0

PD-L1 1-49 %



No. at Risk								
Pembrolizumab combination	103	95	68	50	25	9	1	0
Placebo combination	104	90	66	37	21	6	0	0

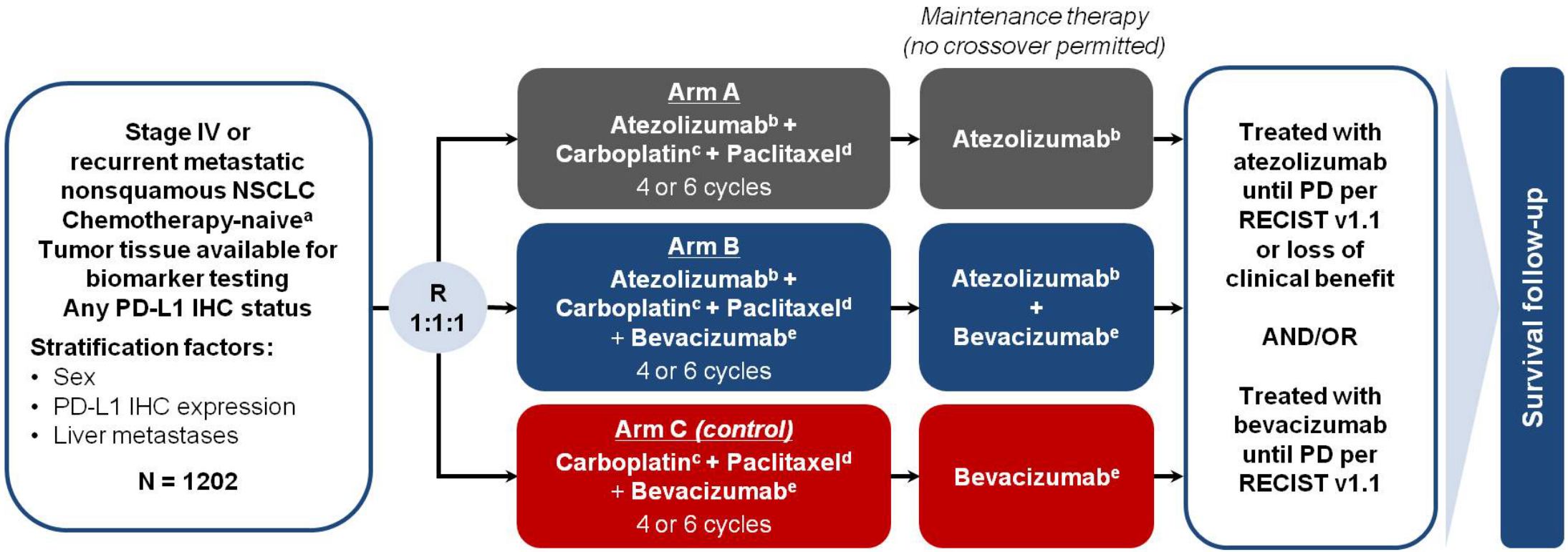
PD-L1 ≥ 50 %



No. at Risk								
Pembrolizumab combination	73	66	53	28	15	3	0	0
Placebo combination	73	60	42	21	9	5	2	0

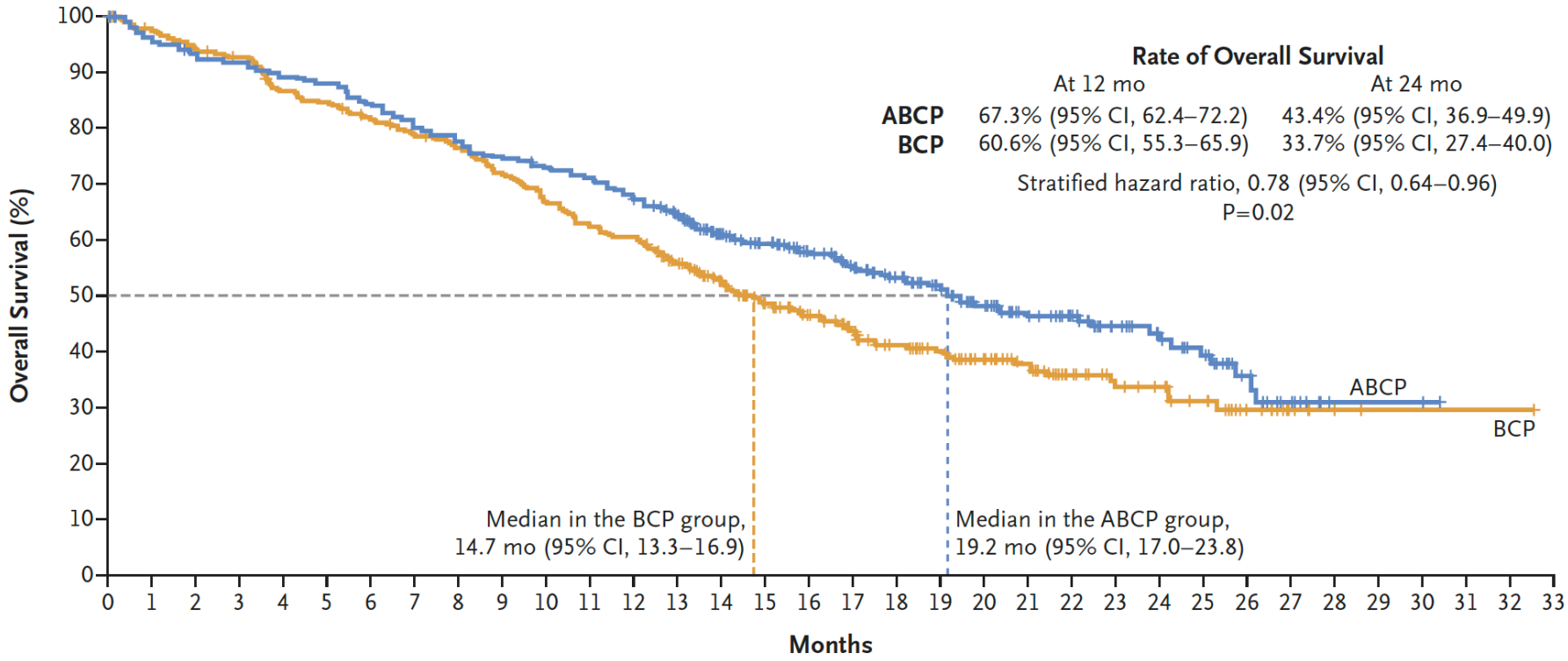
Paz-Ares et al., NEJM 2019

IMpower 150: Atezolizumab/carboplatin/ paclitaxel/bevacizumab vs. carboplatin/paclitaxel/ bevacizumab in advanced non-squamous NSCLC



Socinski et al., AACR 2018

IMpower 150: Atezolizumab/carboplatin/paclitaxel/bevacizumab vs. carboplatin/paclitaxel/bevacizumab in advanced non-squamous NSCLC



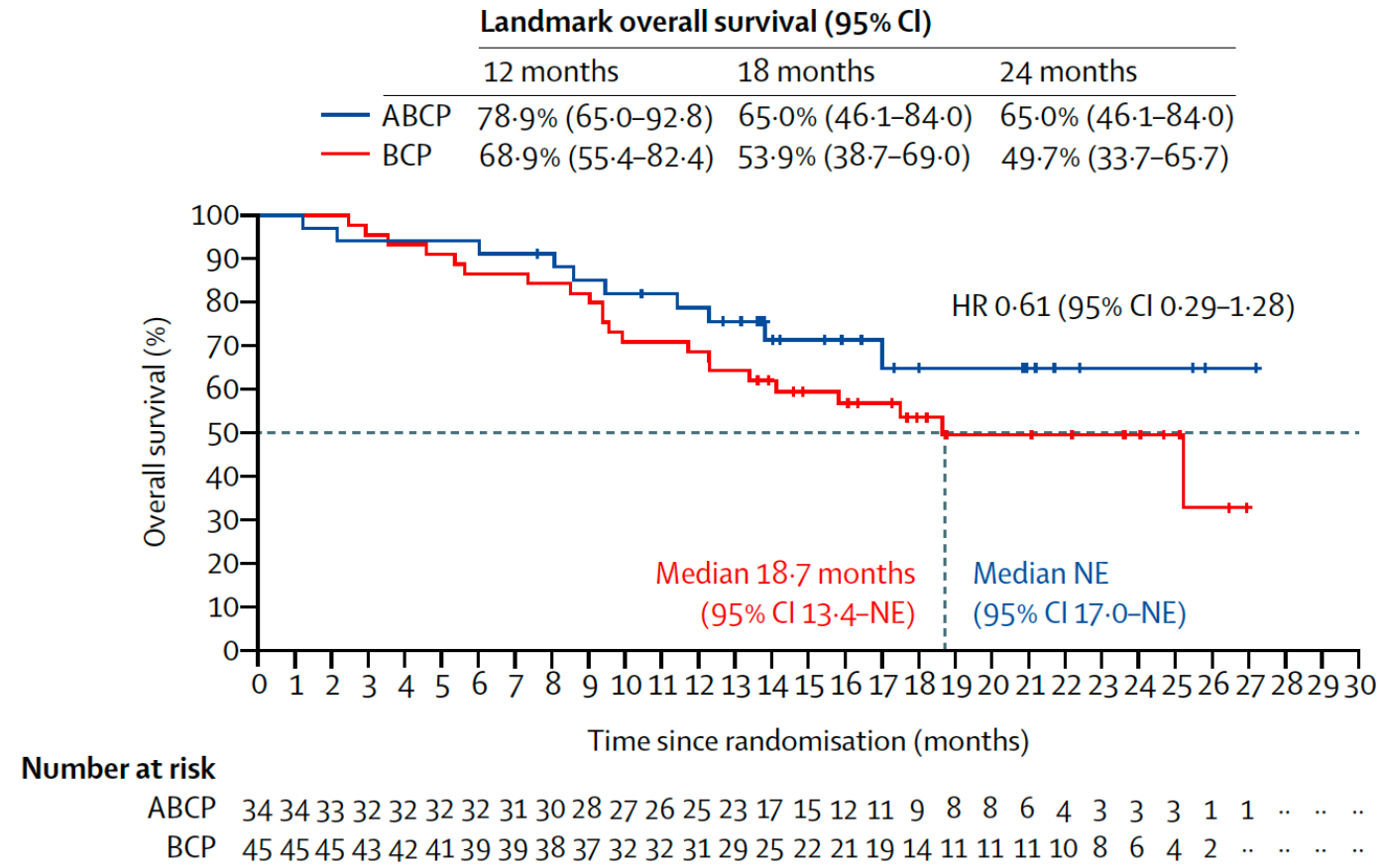
No. at Risk

ABCP	359	339	328	323	314	310	296	284	273	264	256	250	235	218	188	167	147	133	119	103	84	66	57	41	34	28	16	9	2	2	2
BCP	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1

Socinski et al., NEJM 2018

IMpower 150: Subgroup analysis of patients with EGFR mutations

- 34 patients with EGFR mutations treated with ABCP
- ORR = 70.6%
- Median DOR =11.1 months (2.8-18.0)

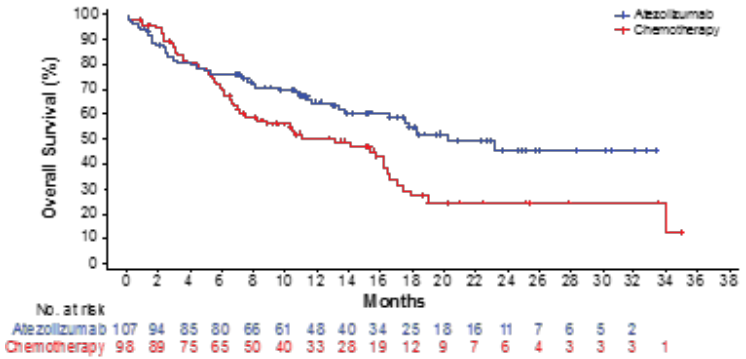


Reck et al., Lancet Respir Med 2019

IMpower110: Atezolizumab vs. chemotherapy in advanced NSCLC

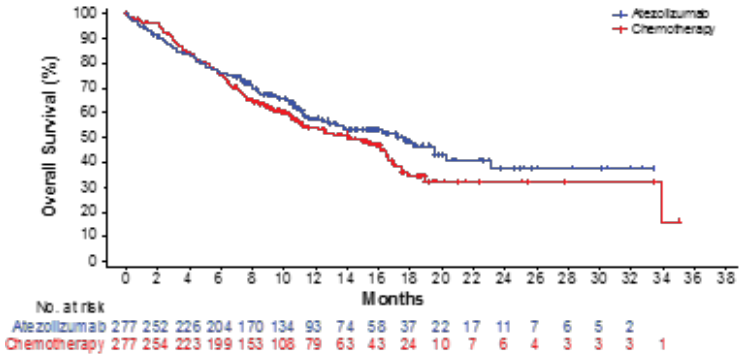
- FDA approval given to PD-L1 ≥ 50% of TC (TC3) or ≥ 10% of IC (IC3)

SP142 (TC3 or IC3-WT)[a]



	Atezo (n = 107)	Chemo (n = 98)
mOS, mo	20.2	13.1
HR[b] (95% CI)	0.59 (0.40, 0.89)	

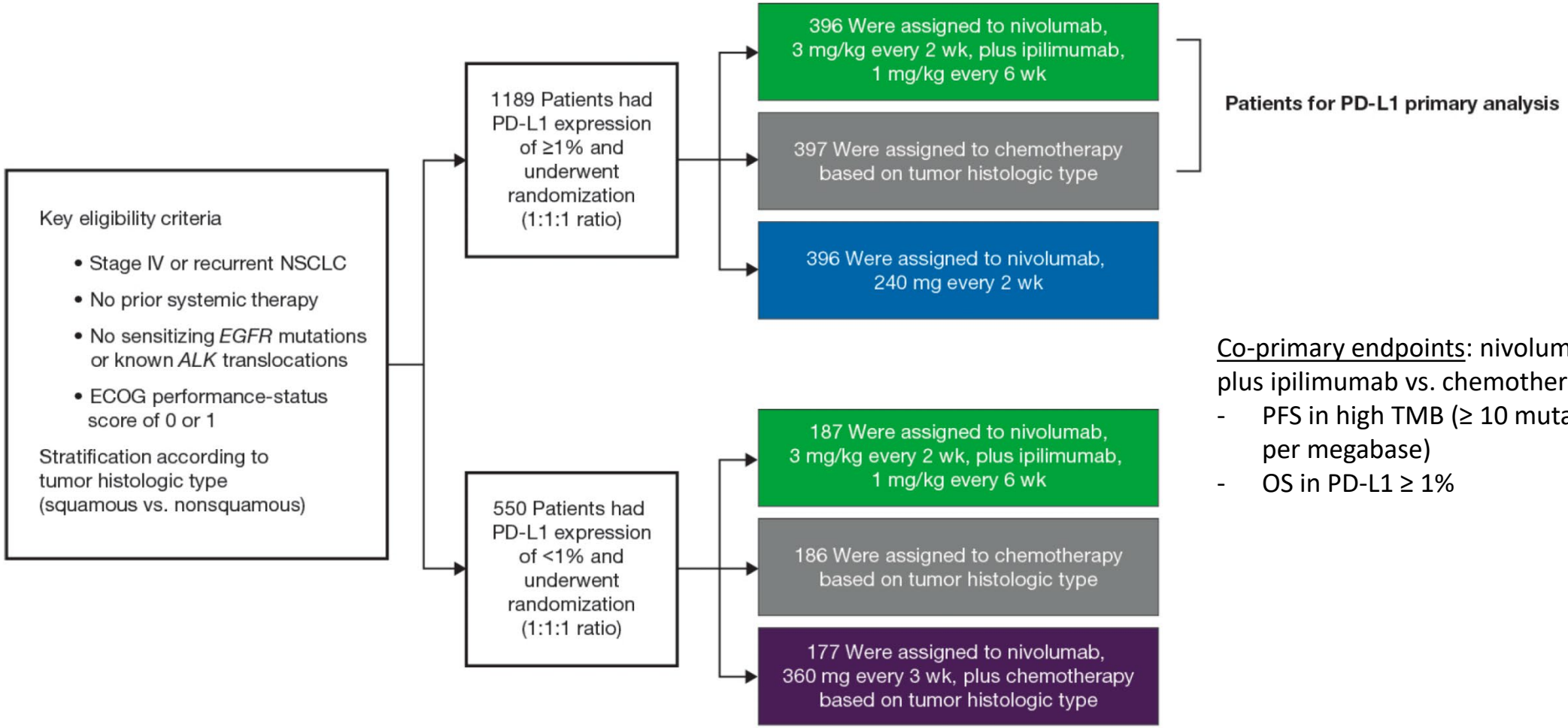
SP142 (TC1/2/3 or IC1/2/3-WT)[a]



	Atezo (n = 277)	Chemo (n = 277)
mOS, mo	17.5	14.1
HR[b] (95% CI)	0.83 (0.65, 1.07)	

Herbst et al., ESMO-IO 2019

CheckMate 227: Dual PD-1 and CTLA-4 blockade using nivolumab and ipilimumab vs. chemotherapy

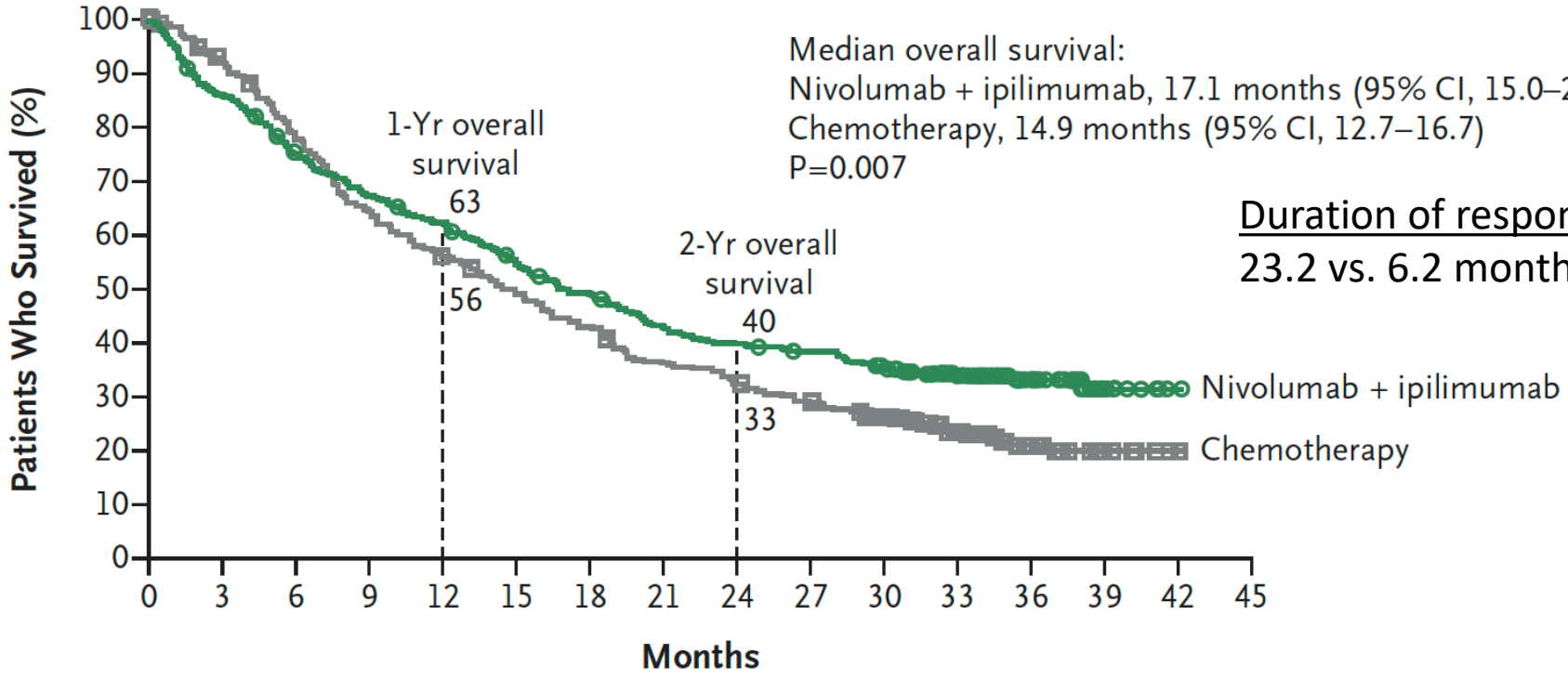


Co-primary endpoints: nivolumab plus ipilimumab vs. chemotherapy
- PFS in high TMB (≥ 10 mutations per megabase)
- OS in PD-L1 ≥ 1%

Hellmann et al., NEJM 2019

CheckMate 227: Dual PD-1 and CTLA-4 blockade using nivolumab and ipilimumab vs. chemotherapy

Overall Survival in Patients with a PD-L1 Expression Level of 1% or More



Duration of response:
23.2 vs. 6.2 months

No. at Risk

Nivolumab + ipilimumab	396	341	295	264	244	212	190	165	153	145	129	91	41	9	1	0
Chemotherapy	397	358	306	250	218	190	166	141	126	112	93	57	22	6	1	0

Hellmann et al., NEJM 2019

CheckMate 9LA: Nivolumab/ipilimumab plus chemotherapy (2 cycles) vs. chemotherapy

Key Eligibility Criteria

- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0-1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)

N = 719

R 1:1

n = 361: **NIVO** 360 mg Q3W + **IPI** 1 mg/kg Q6W + **Chemo[d]** Q3W (2 cycles)

n = 358: **Chemo[d]** Q3W (4 cycles) with optional pemetrexed maintenance (NSQ)

Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

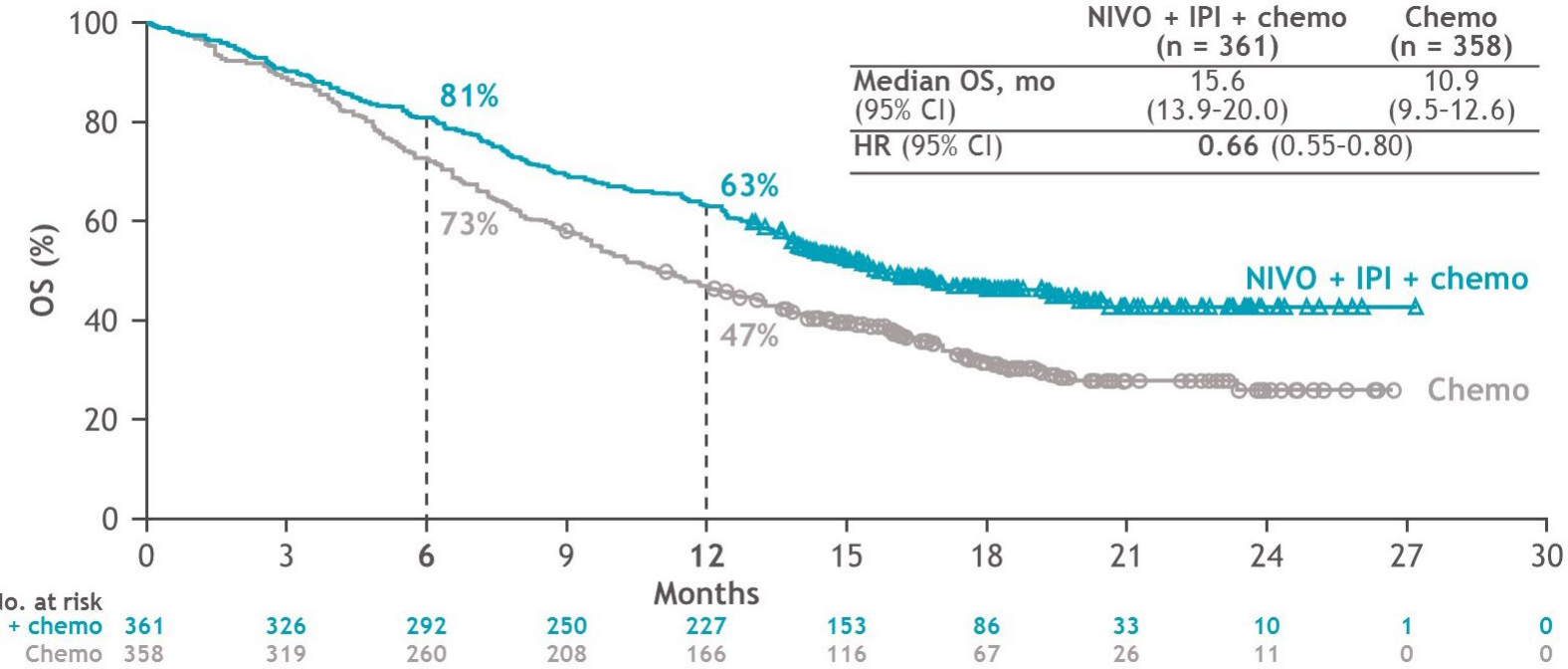
Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Interim database lock: October 3, 2019; minimum follow-up: 8.1 months for OS and 6.5 months for all other endpoints.
Updated database lock: March 9, 2020; minimum follow-up: 12.7 months for OS and 12.2 months for all other endpoints.

[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.

Reck et al., ASCO 2020

CheckMate 9LA: Nivolumab/ipilimumab plus chemotherapy (2 cycles) vs. chemotherapy



	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS, mo (95% CI)	15.6 (13.9-20.0)	10.9 (9.5-12.6)
HR (95% CI)	**0.66** (0.55-0.80)	

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
ORR, n (%)	138 (38)	89 (25)
Odds ratio (95% CI)	1.9 (1.4-2.6)	
BOR, n (%)		
CR	8 (2)	4 (1)
PR	130 (36)	85 (24)
SD	164 (45)	185 (52)
PD	32 (9)	45 (13)
DCR, n (%)	302 (84)	274 (76)

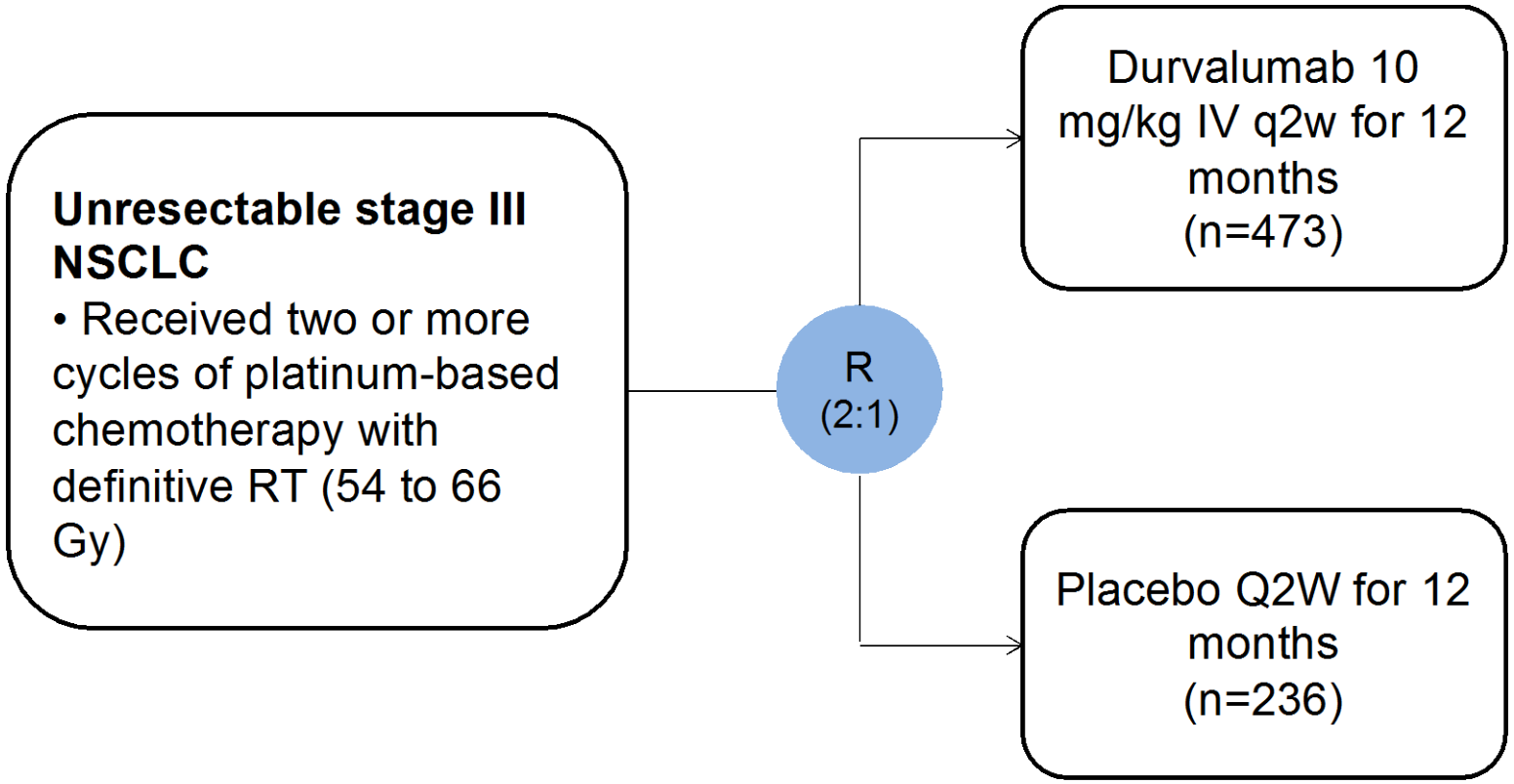
Reck et al., ASCO 2020

Study	Regimen	Study size	Median OS (months)	HR for OS (95% CI)	PD-L1
KEYNOTE 024[1]	Pembrolizumab	305	30 vs. 14.2	0.63 (0.47-0.86)	≥ 50%
KEYNOTE 042[2]	Pembrolizumab	1274	20 vs. 12.2 17.7 vs. 13.0 16.7 vs. 12.1	0.69 (0.56-0.85) 0.77 (0.64-0.92) 0.81 (0.71-0.93)	≥ 50% ≥ 20% ≥ 1%
KEYNOTE 189[3]	Pembrolizumab/ pemetrexed/platinum	616	22 vs. 10.7 NR vs. 10.1 21.8 vs. 12.1 17.2 vs. 10.2	0.56 (0.45-0.70) 0.59 (0.39-0.88) 0.62 (0.42-0.92) 0.52 (0.36-0.74)	All comers ≥ 50% 1-49% < 1%
KEYNOTE 407[4]	Pembrolizumab/ taxane/carboplatin	559	15.9 vs. 11.3 NA NA NA	0.64 (0.49-0.85) 0.64 (0.37-1.10) 0.57 (0.36-0.90) 0.61 (0.38-0.98)	All comers ≥ 50% 1-49% < 1%
IMpower150[5]	Atezolizumab/ bevacizumab/ carboplatin/paclitaxel	1202	19.2 vs. 14.7	0.78 (0.64-0.96)	All comers
IMpower110[6]	Atezolizumab	572	20.2 vs. 13.1 17.5 vs. 14.1	0.59 (0.40-0.89) 0.83 (0.65-1.07)	TC3 or IC3* ≥ 1%
CHECKMATE 227[7]	Nivolumab/ Ipilimumab	1189 (Part 1A)	17.1 vs. 14.9 21.2 vs. 14.0	0.79 (0.65-0.96) 0.70 (0.55-0.90)	≥ 1% ≥ 50%
CHECKMATE 9LA[8]	Nivolumab/ Ipilimumab/ Platinum doublet (2 cycles)	719	15.6 vs. 10.9 18.0 vs. 12.6 15.4 vs. 10.4 15.8 vs. 10.9	0.66 (0.55-0.80) 0.66 (NA) 0.61 (NA) 0.64 (NA)	All comers ≥ 50% 1-49% < 1%

[1]Reck et al., JCO 2019; [2]Mok et al., Lancet 2019; [3]Gadgeel et al., JCO 2020; [4]Paz-Ares et al., NEJM 2018; [5]socinski et al., NEJM 2018; [6]Herbst et al., ESMO IO 2019; [7]Hellmann et al., NEJM 2019; [8]Reck et al. ASCO 2020

* TC3 or IC3: ≥50% expression of PD-L1 on tumor cells (TC3) or ≥10% expression on tumor-infiltrating immune cells (IC3)

PACIFIC: Durvalumab in unresectable stage III NSCLC after chemoradiation



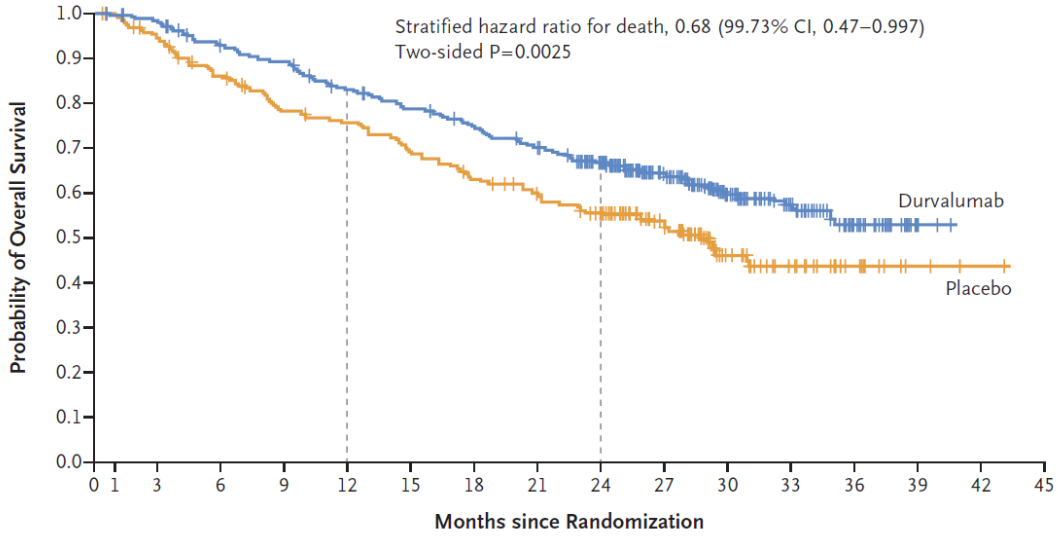
Randomize within 1 to 42 days after CRT

Antonia et al., NEJM 2017

PACIFIC: Durvalumab in unresectable stage III NSCLC after chemoradiation

OS

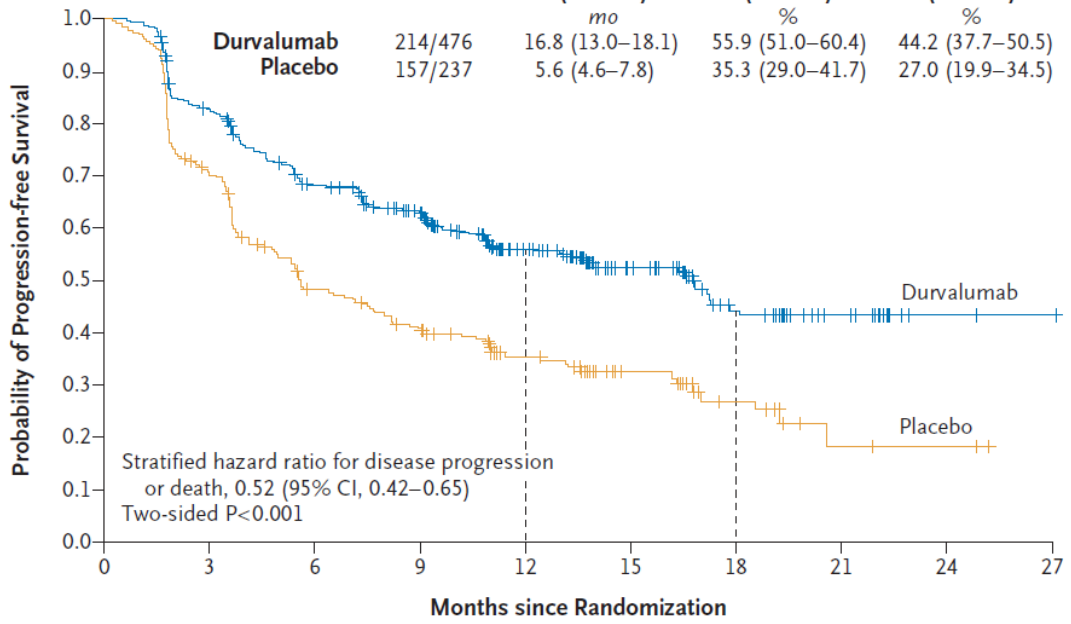
	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



No. at Risk															
Durvalumab	476	464	431	415	385	364	343	319	274	210	115	57	23	2	0	0
Placebo	237	220	198	178	170	155	141	130	117	78	42	21	9	3	1	0

PFS

	No. of Events/ Total No. of Patients	Median PFS (95% CI)	12-Mo PFS (95% CI)	18-Mo PFS (95% CI)
		mo	%	%
Durvalumab	214/476	16.8 (13.0–18.1)	55.9 (51.0–60.4)	44.2 (37.7–50.5)
Placebo	157/237	5.6 (4.6–7.8)	35.3 (29.0–41.7)	27.0 (19.9–34.5)

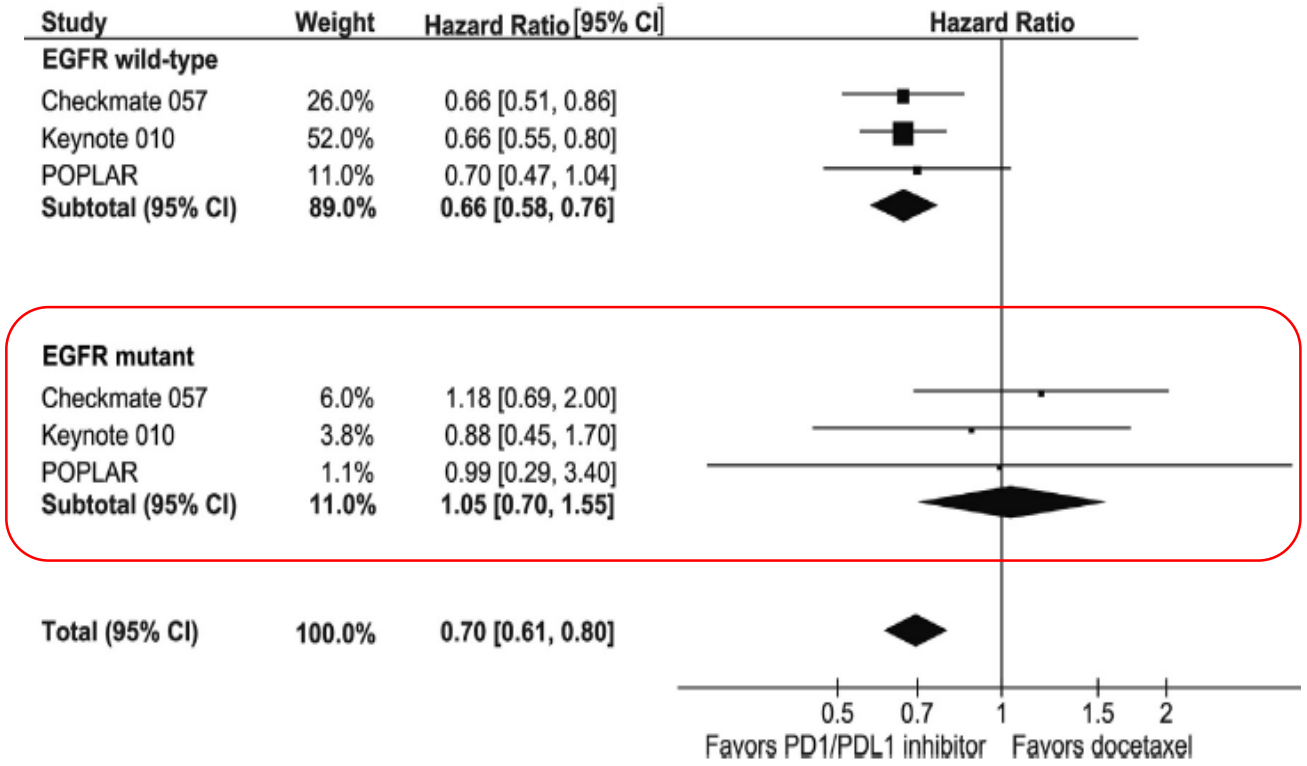


No. at Risk										
Durvalumab	476	377	301	264	159	86	44	21	4	1
Placebo	237	163	106	87	52	28	15	4	3	0

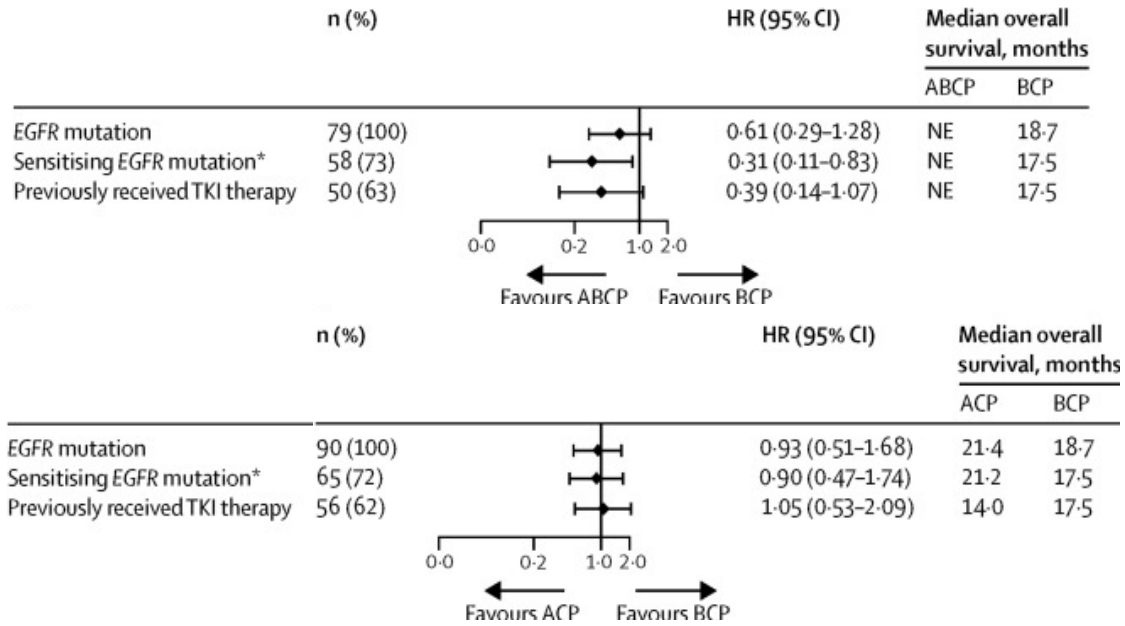
Antonia et al., NEJM 2017 & 2018

Checkpoint inhibitors in metastatic EGFR-mutated NSCLC

Meta-analysis (CheckMate 057, KEYNOTE-010, POPLAR)



IMpower 150



CK Lee et al., JTO 2016
Reck et al., Lancet Resp Med 2019

Approved checkpoint inhibitors in NSCLC

Regimen	Approved	Indication	Dose
Nivolumab	2015	Metastatic Sq NSCLC with progression after chemotherapy (2nd line)	240 mg Q2W or 480 mg Q4W
	2015	Metastatic non-Sq NSCLC with progression after chemotherapy (2nd line)	
Nivolumab + ipilimumab	2020	1st line metastatic NSCLC with PD-L1 ≥1% and no EGFR/ALK mutations	Nivolumab 3 mg/kg Q2W + ipilimumab 1 mg/kg Q6W
Nivolumab + ipilimumab + platinum-doublet	2020	1st line metastatic NSCLC with no EGFR/ALK mutations	Nivolumab 360 mg Q3W + ipilimumab 1 mg/kg Q6W + 2 cycles of chemotherapy

Approved checkpoint inhibitors in NSCLC

Regimen	Approved	Indication	Dose
Pembrolizumab	2015	Metastatic NSCLC with progression after chemotherapy and PD-L1 ≥ 50%	200 mg Q3W or 400 mg Q6W
	2016	Metastatic NSCLC with progression after chemotherapy and PD-L1 ≥ 1%	
	2016	1st line metastatic NSCLC with PD-L1 TPS ≥ 50%	
	2019	1st line stage III NSCLC (not candidate for resection or definitive chemoradiation) and metastatic NSCLC, with PD-L1 TPS ≥ 1% and no EGFR/ALK mutations	
Pembrolizumab + pemetrexed + carboplatin	2017	1st line metastatic non-Sq NSCLC	
Pembrolizumab + pemetrexed + platinum	2018	1st line metastatic non-Sq NSCLC with no EGFR/ALK mutations	
Pembrolizumab + carboplatin + paclitaxel/nab-paclitaxel	2018	1st line metastatic Sq NSCLC	

Approved checkpoint inhibitors in NSCLC

Regimen	Approved	Indication	Dose
Atezolizumab	2016	Metastatic NSCLC with progression after platinum chemotherapy and targeted therapy if EGFR/ALK mutation-positive	840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W
Atezolizumab + bevacizumab + paclitaxel + carboplatin	2018	1st line metastatic non-Sq NSCLC with no EGFR/ALK mutations	For 4-6 cycles: atezolizumab 1200 mg Q3W + chemotherapy + bevacizumab Maintenance: 840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W
Durvalumab	2018	Stage III NSCLC, ineligible for surgery and without progression after chemoradiation	10 mg/kg Q2W
Atezolizumab + nab-paclitaxel + carboplatin	2019	1st line metastatic non-Sq NSCLC with no EGFR/ALK mutations	For 4-6 cycles: atezolizumab 1200 mg Q3W + chemotherapy Maintenance: 840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W
Atezolizumab	2020	1st line metastatic NSCLC with PD-L1 ≥ 50% of tumor cells or ≥ 10% of immune cells with no EGFR/ALK mutations	840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W

Small-cell lung cancer

- 10-15% of lung cancers
- Highly correlated with smoking
- Median survival 14-20 months in LS-SCLC and 8-13 months in ES-SCLC[1]
- Until recently, only FDA approved 2nd line option: topotecan (approved in 1998)
- Recent approvals of immunotherapies mark the first progress in decades

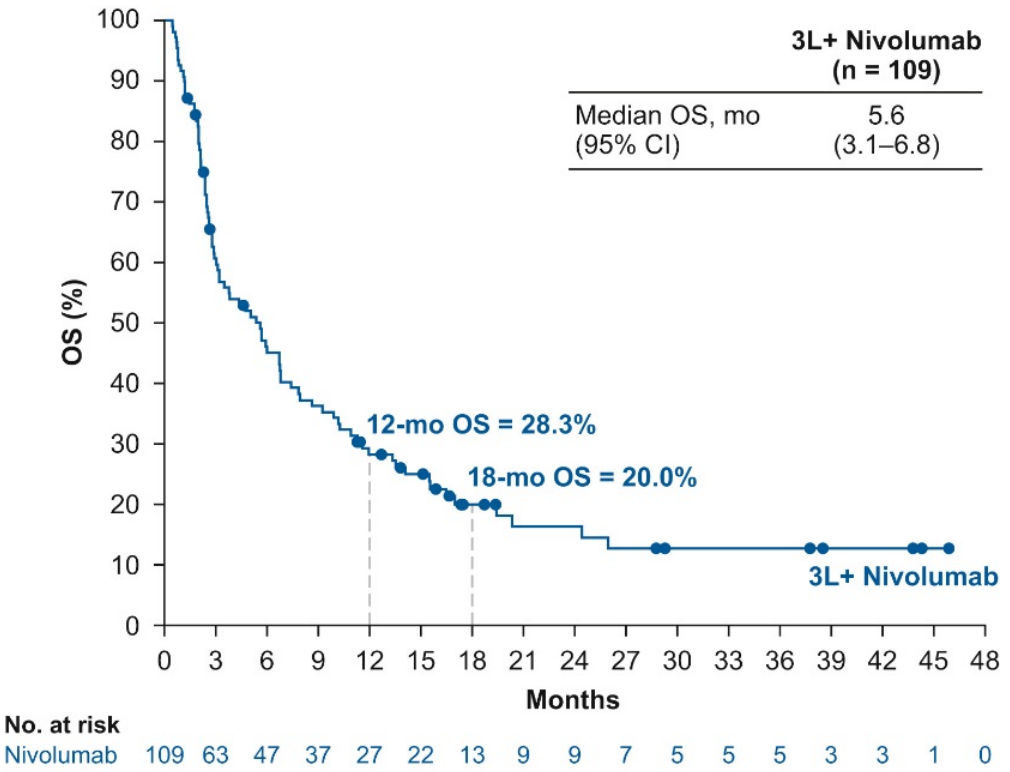
[1]Demedts et al., EUR RESPIR J 2020

Approved checkpoint inhibitors in SCLC

Regimen	Approved	Indication	Dose
Nivolumab	2018	Metastatic SCLC with progression on platinum chemotherapy and one other therapy (3rd line)	240 mg Q2W
Pembrolizumab	2019	Metastatic SCLC with progression on platinum chemotherapy and one other therapy (3rd line)	200 mg Q3W
Atezolizumab + carboplatin + etoposide	2019	1st line ES-SCLC	For 4 cycles: atezolizumab 1200 mg + chemotherapy Q3W Maintenance: 840 mg Q2W, 1200 mg Q3W, or 1680 mg Q4W
Durvalumab + etoposide + carboplatin/cisplatin	2020	1st line ES-SCLC	Combination: durvalumab 1500 mg + chemotherapy Q3W Maintenance: durvalumab 1500 mg Q4W

CheckMate 032: Nivolumab in 3rd line SCLC

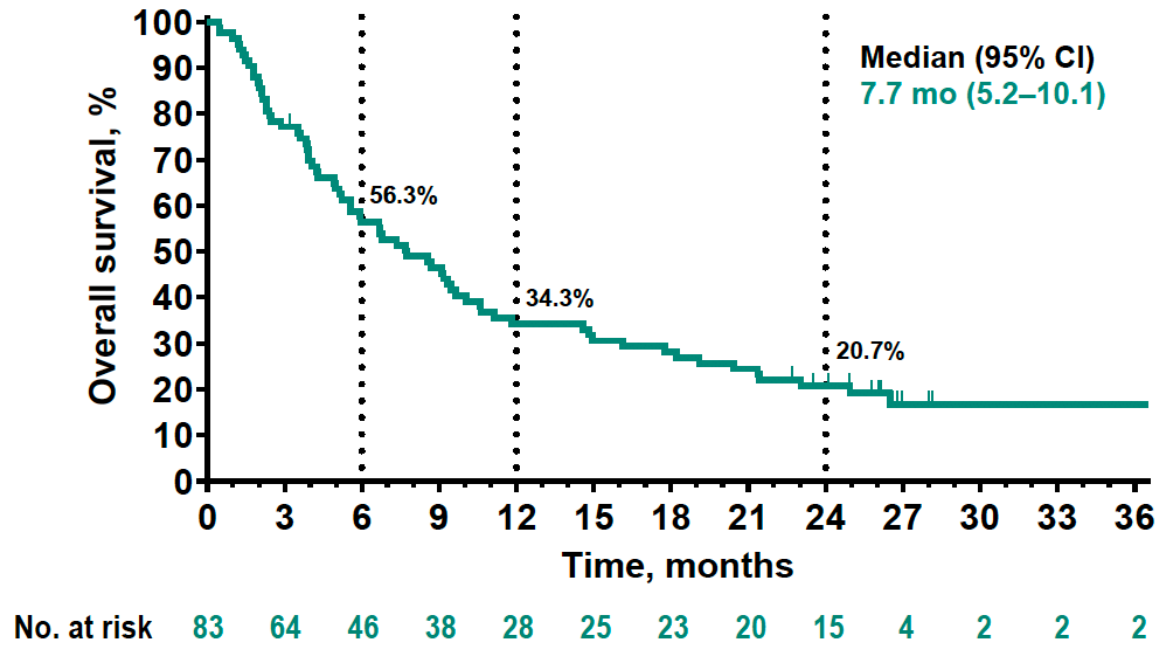
- Nivolumab in recurrent SCLC with progression progression after two or more chemotherapy regimens
- Nivolumab 3 mg/kg Q2W
- Median follow-up: 28.3 months
- ORR: 11.9%
- Median DOR: 17.9 months (range 3.0-42.1)
- Median OS: 5.6 months (3.1-6.8)
- Median PFS: 1.4 months (1.3-1.6)



Ready et al., JTO 2019

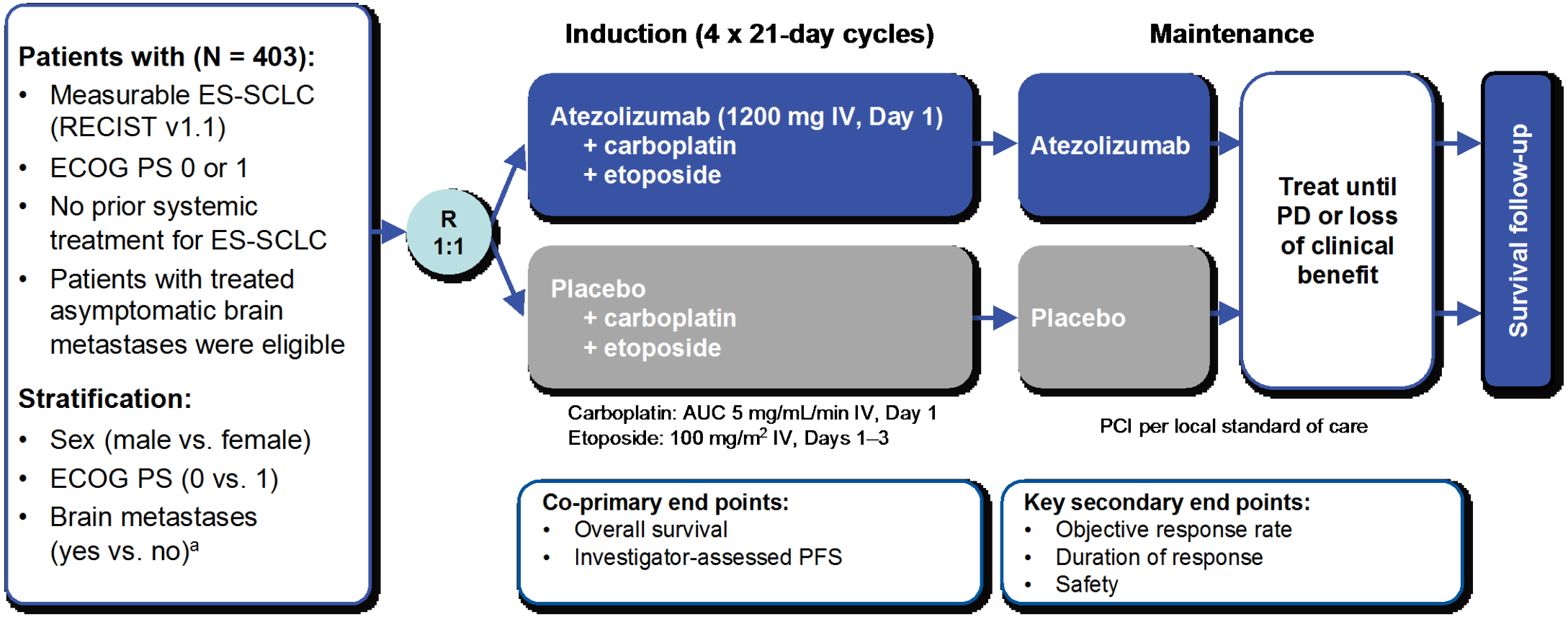
Pembrolizumab in 3rd line SCLC

- Combined analysis of 83 patients from KEYNOTE-028 (PD-L1+ only) and KEYNOTE-158 (Cohort C1)
- ORR: 19.3%
- Median DOR: NR (4.1-35.8 months)
- Median OS: 7.7 months (5.2-10.1)
- Median PFS: 2.0 months (1.9-3.4)



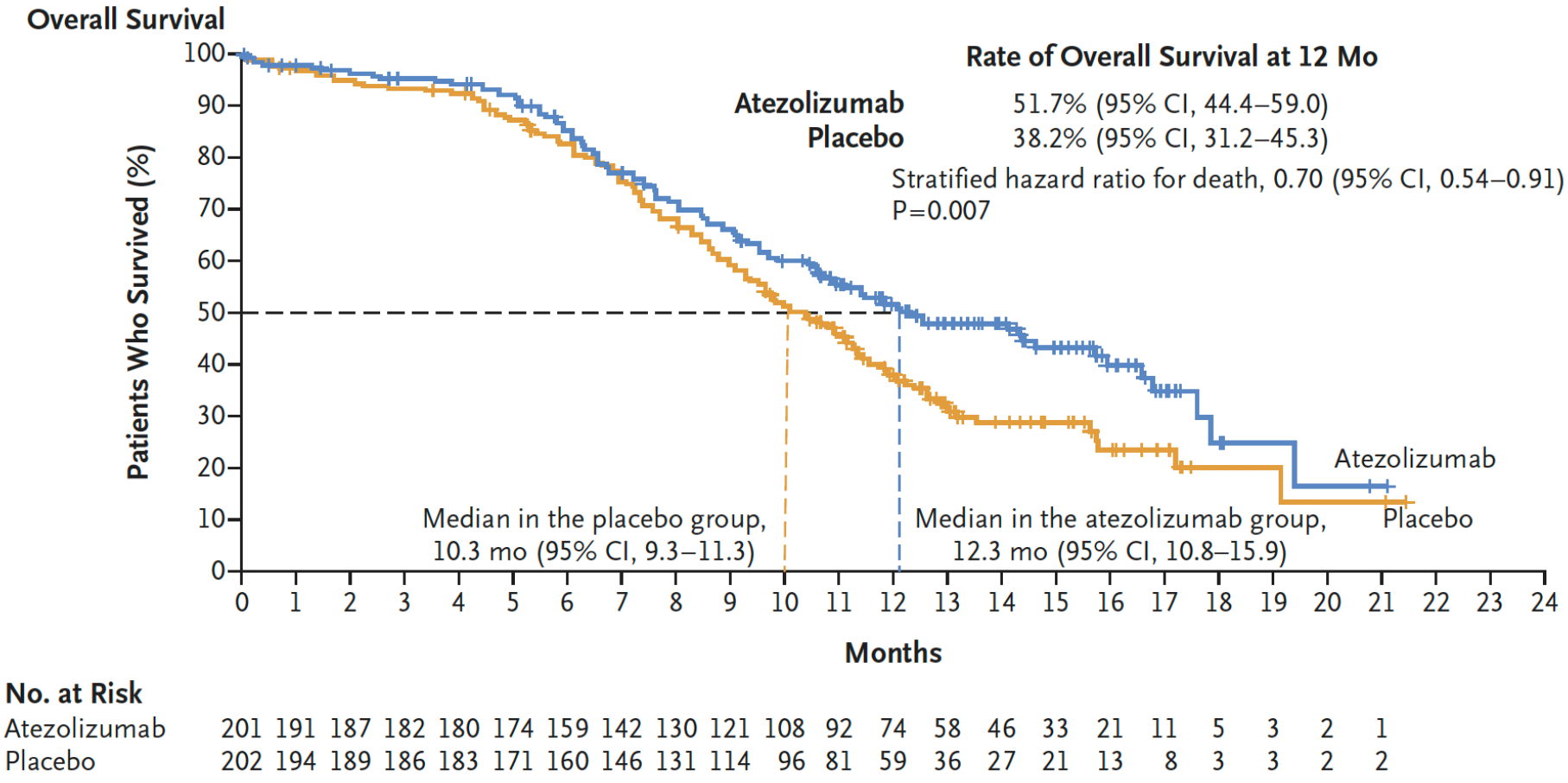
Chung et al., JTO 2020
Ott et al., JCO 2017

IMpower133: Atezolizumab plus chemotherapy vs. chemotherapy in ES-SCLC



Liu et al., IASLC 2018

IMpower133: Atezolizumab plus chemotherapy vs. chemotherapy in ES-SCLC



Horn et al., NEJM 2018

CASPIAN: Durvalumab plus chemotherapy vs. chemotherapy in ES-SCLC

- Treatment-naïve ES-SCLC
- WHO PS 0 or 1
- Asymptomatic or treated and stable brain metastases permitted
- Life expectancy ≥12 weeks
- Measurable disease per RECIST v1.1

N=805 (randomised)

1:1:1

R

Stratified by planned platinum agent (carboplatin vs cisplatin)

Durvalumab + EP*
Durvalumab 1500 mg + EP q3w for up to 4 cycles

→ **Durvalumab**
1500 mg q4w until disease progression

EP*
q3w for up to 6 cycles†

→ **Optional PCI†**

Durvalumab + tremelimumab + EP*
Durvalumab 1500 mg + tremelimumab 75 mg + EP q3w for up to 4 cycles

→ **Durvalumab‡**
1500 mg q4w until disease progression

Primary endpoint

- OS

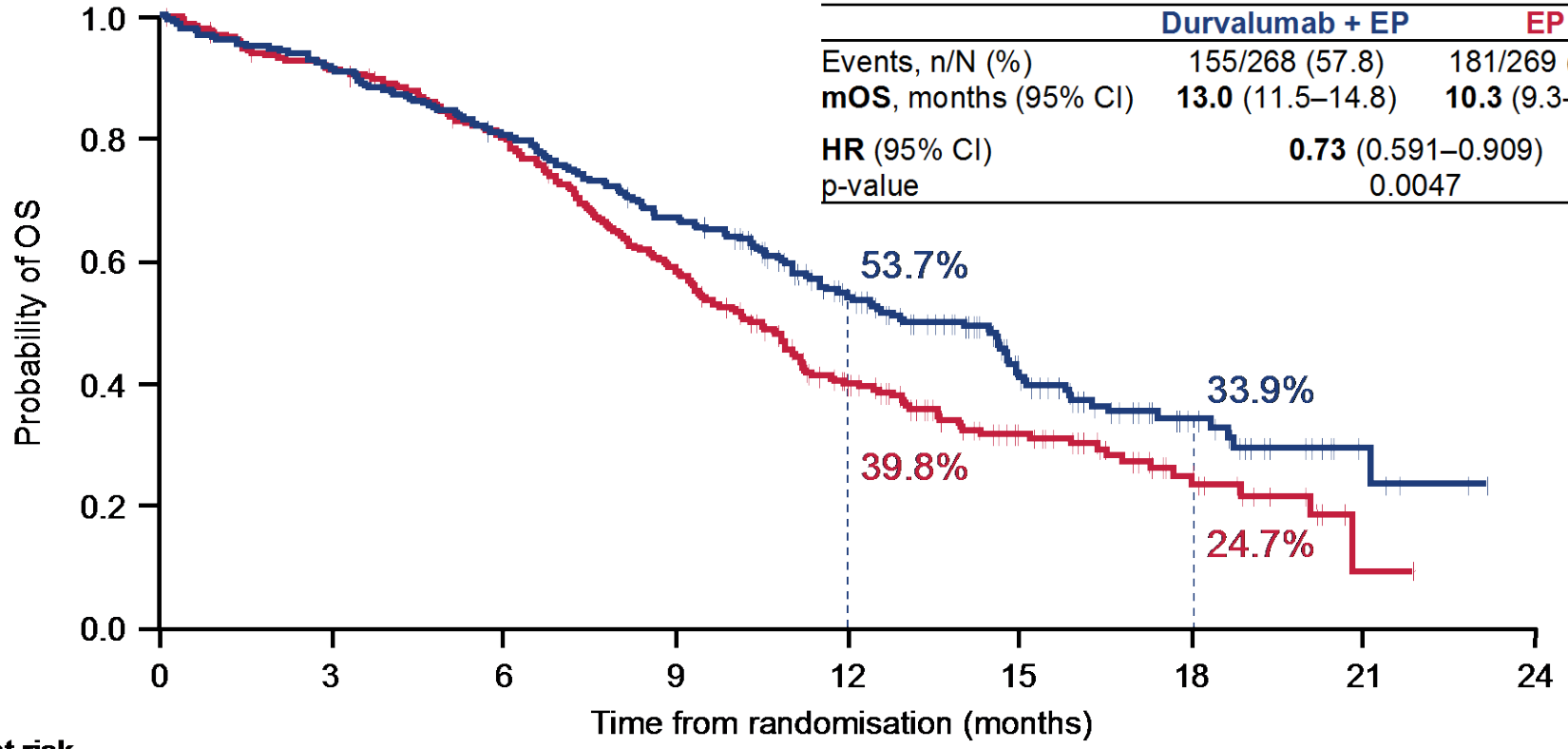
Secondary endpoints

- PFS
- ORR
- Safety & tolerability
- Health-related QoL

Paz-Ares et al., IASLC 2019

CASPIAN: Durvalumab plus chemotherapy vs. chemotherapy in ES-SCLC

	Durvalumab + EP	EP
Events, n/N (%)	155/268 (57.8)	181/269 (67.3)
mOS, months (95% CI)	**13.0** (11.5–14.8)	**10.3** (9.3–11.2)
HR (95% CI)	**0.73** (0.591–0.909)	
p-value	0.0047	



No. at risk									
Durvalumab + EP	268	244	214	177	116	57	25	5	0
EP	269	242	209	153	82	44	17	1	0

Paz-Ares et al., IASLC 2019

Conclusions

- Immune checkpoint inhibitor (ICI) therapy has transformed the treatment landscape for stage III/IV NSCLC and ES-SCLC.
- Predictive biomarkers to better select patients who benefit from ICI therapy are needed.

Resources

Brahmer *et al. Journal for ImmunoTherapy of Cancer* (2018) 6:75
https://doi.org/10.1186/s40425-018-0382-2

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES **Open Access**

The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of non-small cell lung cancer (NSCLC)

Julie R. Brahmer[1], Ramaswamy Govindan[2], Robert A. Anders[3], Scott J. Antonia[4], Sarah Sagorsky[5], Marianne J. Davies[6], Steven M. Dubinett[7], Andrea Ferris[8], Leena Gandhi[9], Edward B. Garon[10], Matthew D. Hellmann[11], Fred R. Hirsch[12], Shakuntala Malik[13], Joel W. Neal[14], Vassiliki A. Papadimitrakopoulou[15], David L. Rimm[16], Lawrence H. Schwartz[17], Boris Sepesi[18], Beow Yong Yeap[19], Naiyer A. Rizvi[20] and Roy S. Herbst[21*]

Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Case Studies

Case Study 1

A 55-year-old female with light smoking history presented with dyspnea and fatigue. During work-up, she was found to have a large pericardial effusion, marantic endocarditis, innumerable pulmonary nodules, and bilateral pleural effusions. She underwent pericardiocentesis (750 cc removed). Pathology of pericardial effusion was consistent with lung adenocarcinoma. Brain MRI was negative. You ordered tissue molecular testing. You saw her on inpatient service. What would you do?

A) Start pembrolizumab

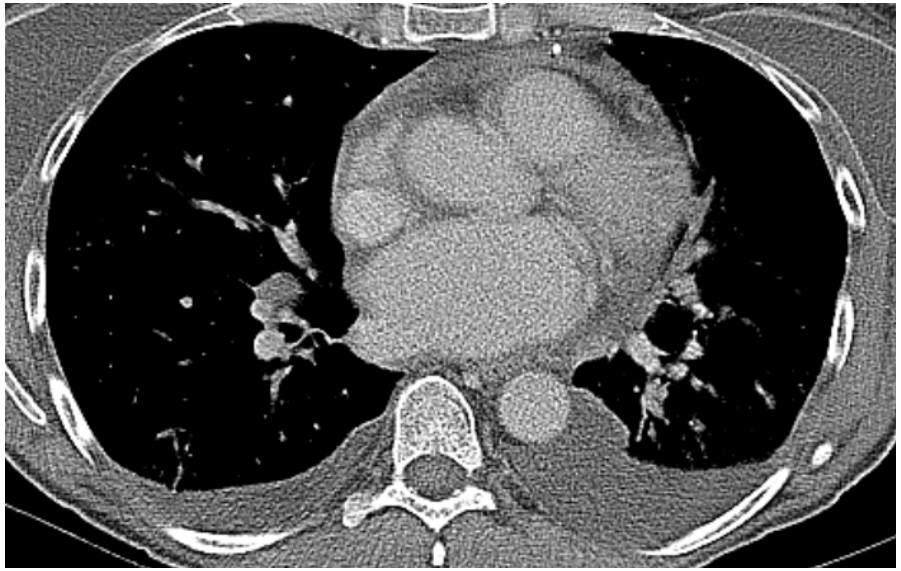
B) Start carboplatin, pemetrexed, pembrolizumab

C) Wait for molecular testing results prior to starting systemic therapy

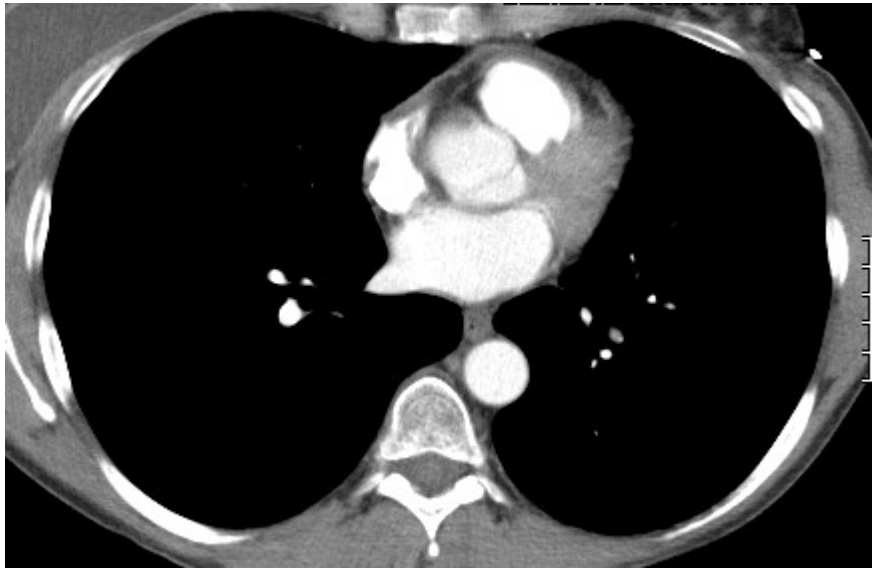
D) Start carboplatin, pemetrexed while awaiting the NGS results

Case Study 1

- NGS came back one day after cycle 2 of carboplatin and pemetrexed and showed the following: KRAS G12A and TP53 mutations. PD-L1 10% by 22c3, 5% by 28-8.



At initial presentation



After 2 cycles of chemotherapy

Case Study 1

- What is the best next step among the options below?

  A) Continue carboplatin/pemetrexed, followed by pemetrexed maintenance therapy

  B) Add pembrolizumab to carboplatin/pemetrexed

  C) Stop chemotherapy and explore clinical trials targeting KRAS mutations

Case Study 2

- A 59-year-old never-smoker female presented with dyspnea. CT showed a massive right pleural effusion, an endobronchial lesion, and mediastinal lymphadenopathy. She underwent thoracentesis and pathology showed findings consistent with lung adenocarcinoma. Analysis of pleural effusion showed PD-L1 100%, but no further testing was possible due to insufficient tumor cells. She underwent bronchoscopy and mutation testing done on a lymph node showed EGFR L858R. Brain MRI negative. How would you treat this patient?

  A) Pembrolizumab

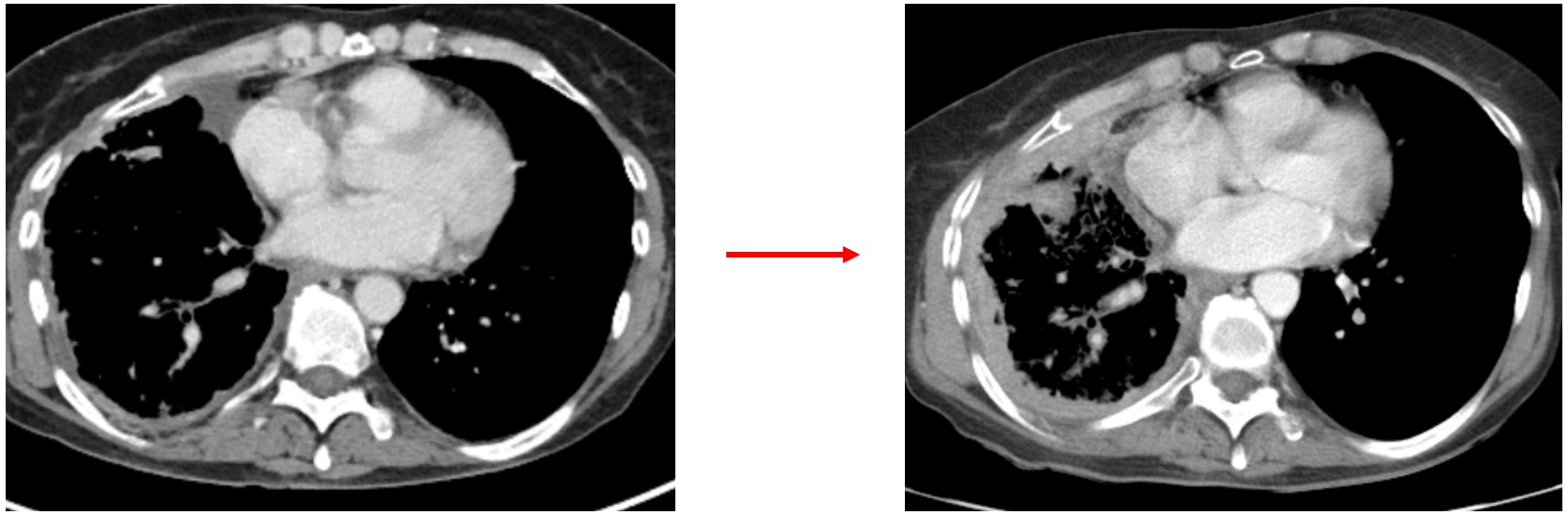
  B) Carboplatin, pemetrexed

  C) Carboplatin, paclitaxel, bevacizumab, atezolizumab

  D) Osimertinib

Case Study 2

- She started osimertinib 80 mg QD.



At initial presentation

3 months after osimertinib

- ctDNA testing showed increased allele frequencies of EGFR and TP53. A repeat tissue biopsy showed the same mutations.

Case Study 2

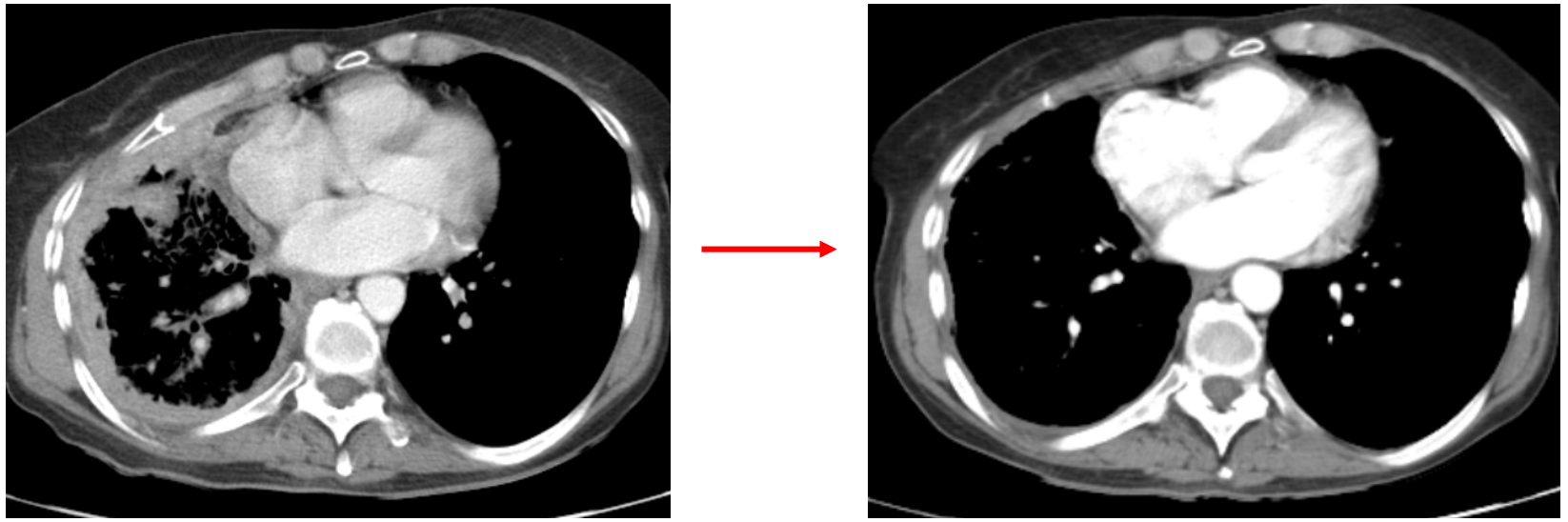
- What is the best next step (more than one answer may apply)?

  A) Start pembrolizumab

  B) Switch treatment to carboplatin, pemetrexed +/- osimertinib

  C) Switch treatment to carboplatin, paclitaxel, atezolizumab, bevacizumab

  D) Switch treatment to docetaxel plus ramucirumab



Thank you for your attention

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