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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

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Disclosures

- Consulting Fees: DynaMed, Advance Medical/TelaDoc Health, Astra Zeneca
- Contracted Research: Bristol Meyer Squibb, Abbvie/Stemcentrx, Novocure
- 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)
- NSCLC has relatively long and extensive history of immunotherapy use

Estimated Deaths

Male		
Lung & bronchus	76,650	24%
Prostate	31,620	10%
Colon & rectum	27,640	9%
Pancreas	23,800	7%
Liver & intrahepatic bile duct	21,600	7%
Leukemia	13,150	4%
Esophagus	13,020	4%
Urinary bladder	12,870	4%
Non-Hodgkin lymphoma	11,510	4%
Brain & other nervous system	9,910	3%
All sites	**321,670**	

Female		
Lung & bronchus	66,020	23%
Breast	41,760	15%
Colon & rectum	23,380	8%
Pancreas	21,950	8%
Ovary	13,980	5%
Uterine corpus	12,160	4%
Liver & intrahepatic bile duct	10,180	4%
Leukemia	9,690	3%
Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	7,850	3%
All sites	**285,210**	

American Cancer Society

FDA-approved checkpoint inhibitors in lung cancer

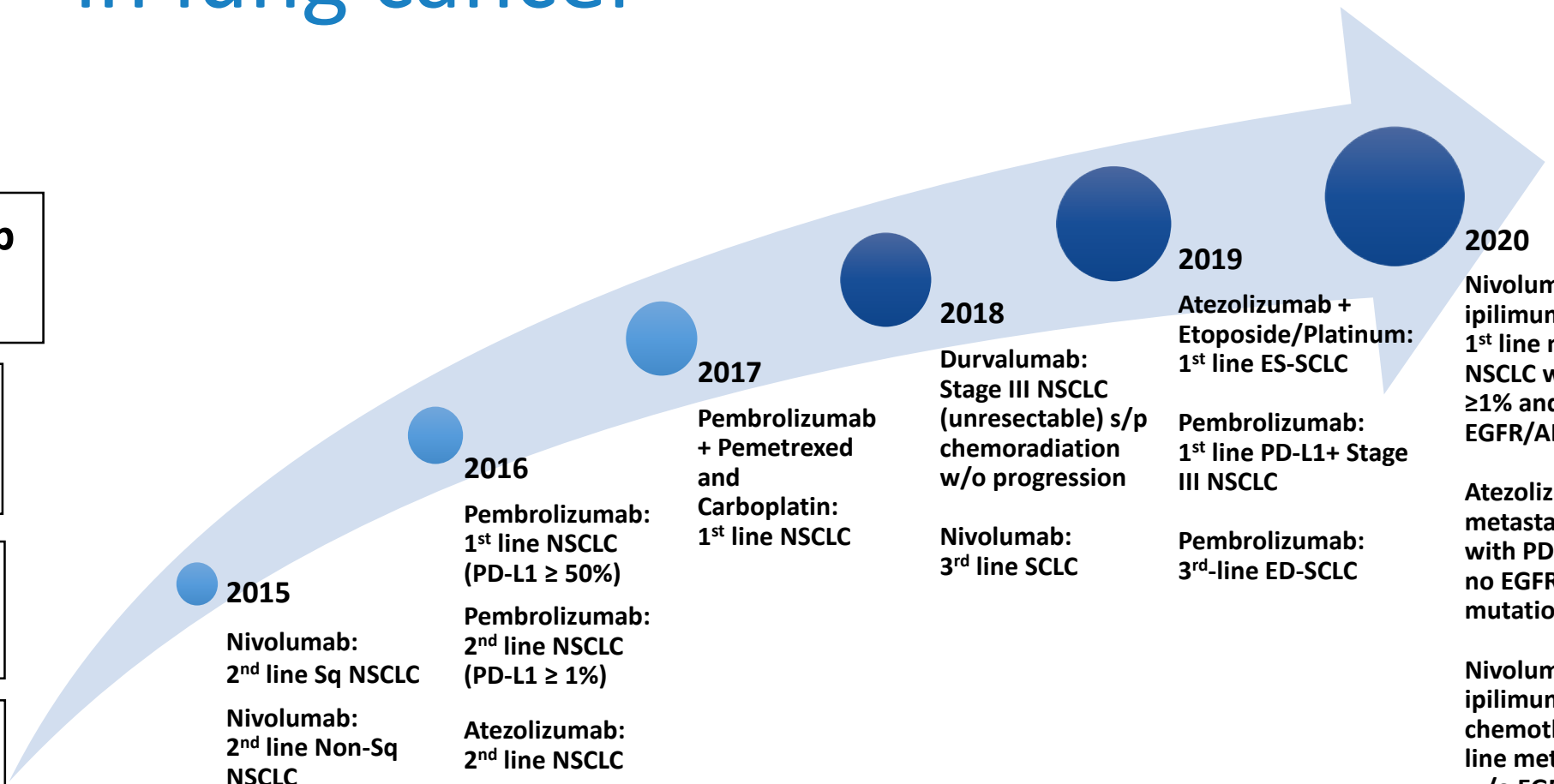
Nivolumab
PD-1

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 NSCLC

2018

Durvalumab: Stage III NSCLC (unresectable) s/p chemoradiation w/o progression

Nivolumab: 3rd line SCLC

2019

Atezolizumab + Etoposide/Platinum: 1st line ES-SCLC

Pembrolizumab: 1st line PD-L1+ Stage III NSCLC

Pembrolizumab: 3rd-line ED-SCLC

2020

Nivolumab + ipilimumab: 1st line metastatic NSCLC with PD-L1 ≥1% and no EGFR/ALK mutations

Atezolizumab: 1st line metastatic NSCLC with PD-L1 ≥50% and no EGFR/ALK mutations

Nivolumab + ipilimumab + chemotherapy: 1st line metastatic NSCLC w/o EGFR/ALK mutations

Approved checkpoint inhibitors in NSCLC

Drug	Approved	Indication	Dose
Nivolumab	2015	Metastatic Squamous NSCLC with progression after chemotherapy (2nd line)	240 mg Q2W or 480 mg Q4W
	2015	Metastatic Non-Squamous 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

Drug	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-Squamous NSCLC	
Pembrolizumab + pemetrexed + platinum	2018	1st line metastatic Non-Squamous NSCLC with no EGFR/ALK mutations	
Pembrolizumab + carboplatin + paclitaxel/nab-paclitaxel	2018	1st line metastatic Squamous NSCLC	

Approved checkpoint inhibitors in NSCLC

Drug	Approved	Indication	Dose
Atezolizumab	2016	Metastatic NSCLC with progression after Pt-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-squamous 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-squamous 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

Treatment Naïve Regimens: Competing Strategies in NSCLC

- **KEYNOTE 024** – Pembrolizumab vs. Chemotherapy in PD-L1 ≥ 50%
- **KEYNOTE 042** – Pembrolizumab vs. Chemotherapy in PD-L1 ≥ 1%
- **KEYNOTE 189** – Pembrolizumab + Chemotherapy vs. Chemotherapy alone in advanced non-squamous NSCLC
- **IMPOWER150** – Atezolizumab + Chemotherapy (Bev) vs. Chemotherapy (Bev) in advanced non-squamous NSCLC
- **KEYNOTE 407** – Pembrolizumab + Chemotherapy vs. Chemotherapy in advanced squamous cell lung cancer
- **CHECKMATE 227** – Ipilimumab + Nivolumab vs. Chemotherapy in advanced NSCLC with high TMB
- **IMPOWER110** – Atezolizumab vs. chemotherapy in PD-L1 ≥ 1%

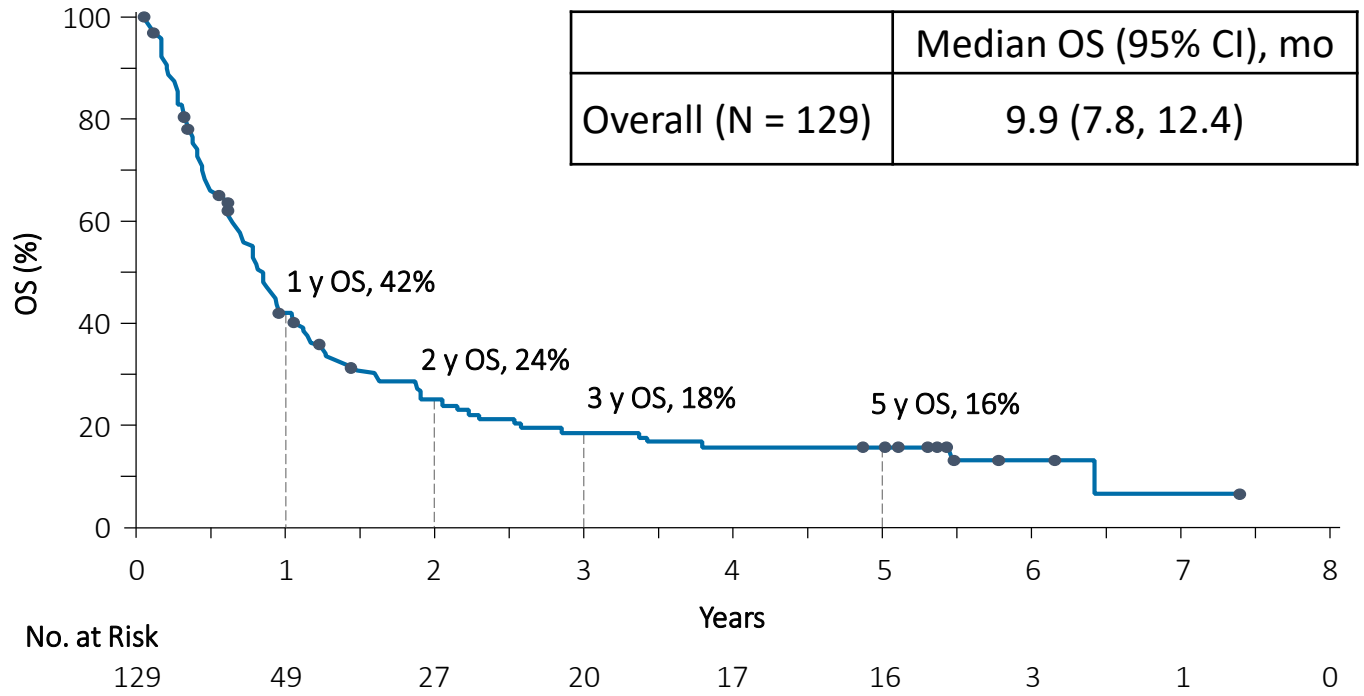
CA209-003: Nivolumab in Heavily-pretreated Advanced NSCLC (NCT00730639)

Phase 1, 5-Year Update

- 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

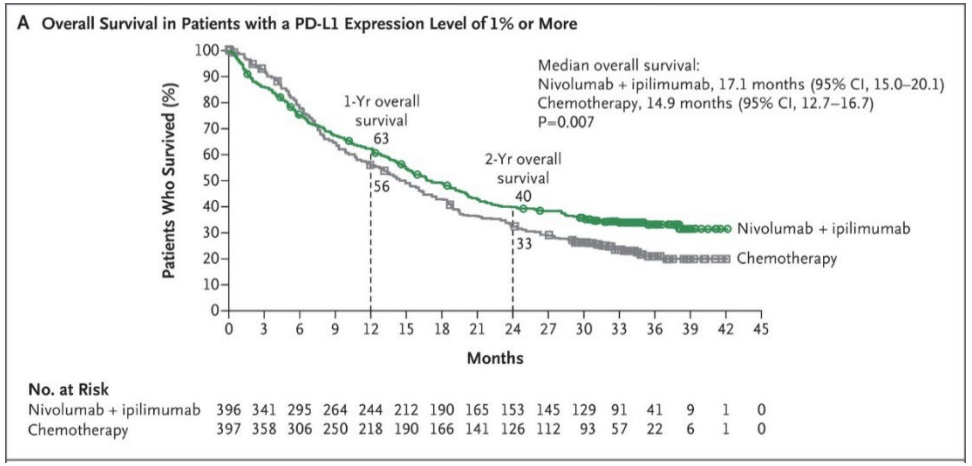
	Median OS (95% CI), mo
Overall (N = 129)	9.9 (7.8, 12.4)

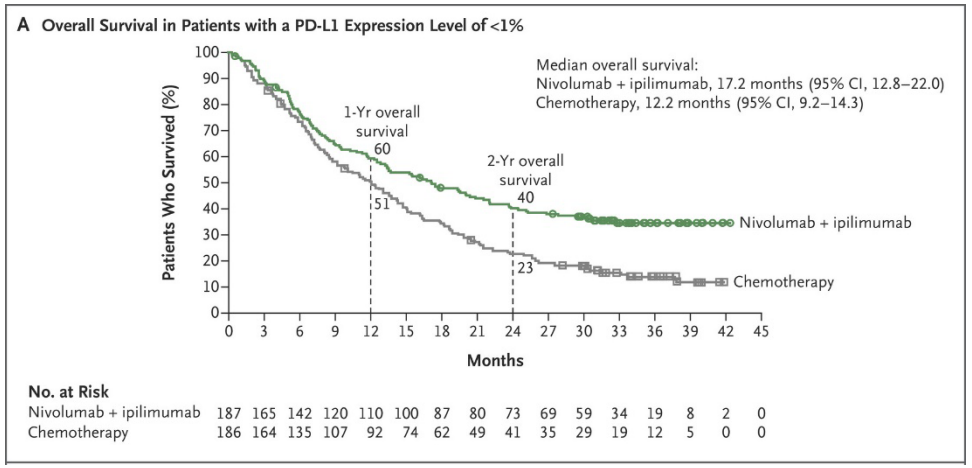


Gettinger et al. JCO 2018
Brahmer et al, AACR 2017
NCI SEER data, Lung and Bronchus Cancer, 2014

CheckMate 227

- Primary endpoint: OS in PD-L1 ≥ 1% (tumor cells)
  - Nivo/ipi: 17.1 months
  - Chemo: 14.9 months
- Longer duration of response with nivo/ipi over chemo
- Benefit of nivolumab + ipilimumab seen regardless of PD-L1 status in this study





Hellmann, NEJM 2019.

CheckMate 9LA: Nivolumab/Ipilimumab + limited chemo

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

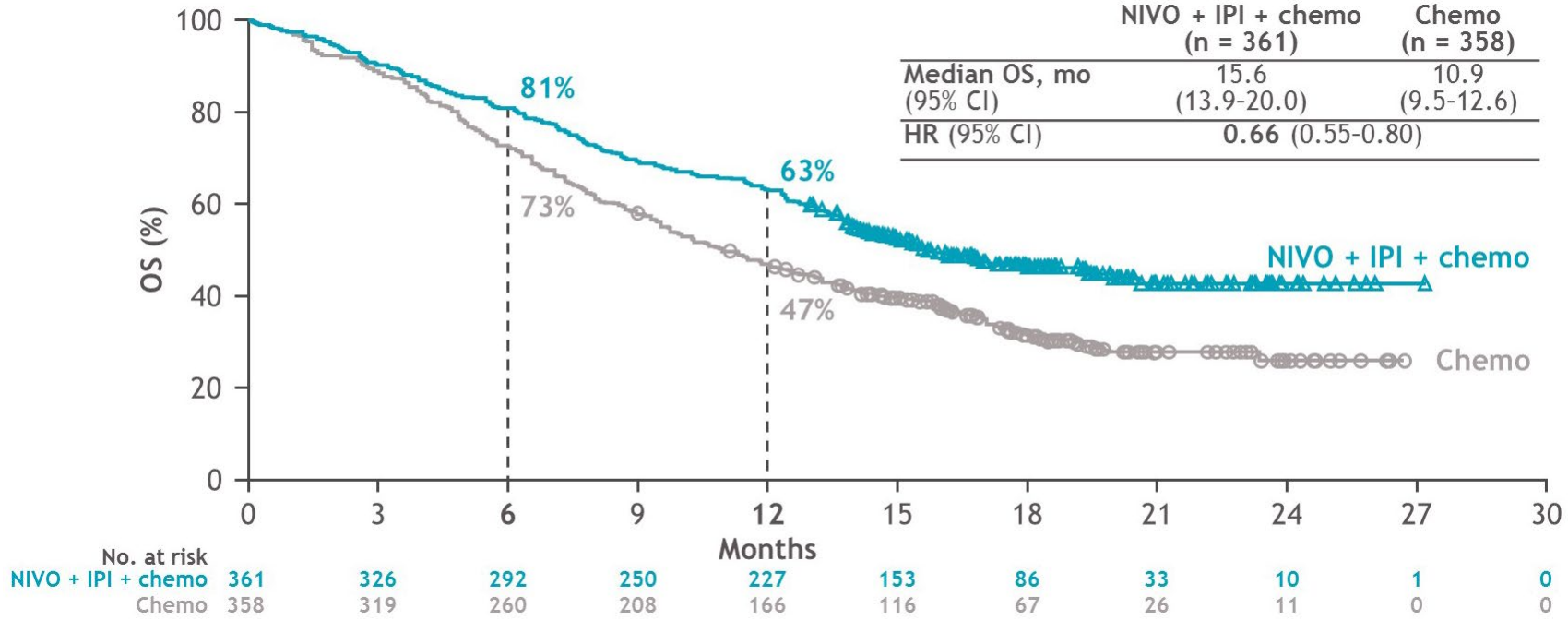
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

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 M et al, ASCO 2020.

CheckMate 9LA: Nivolumab/Ipilimumab + limited chemo



	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)

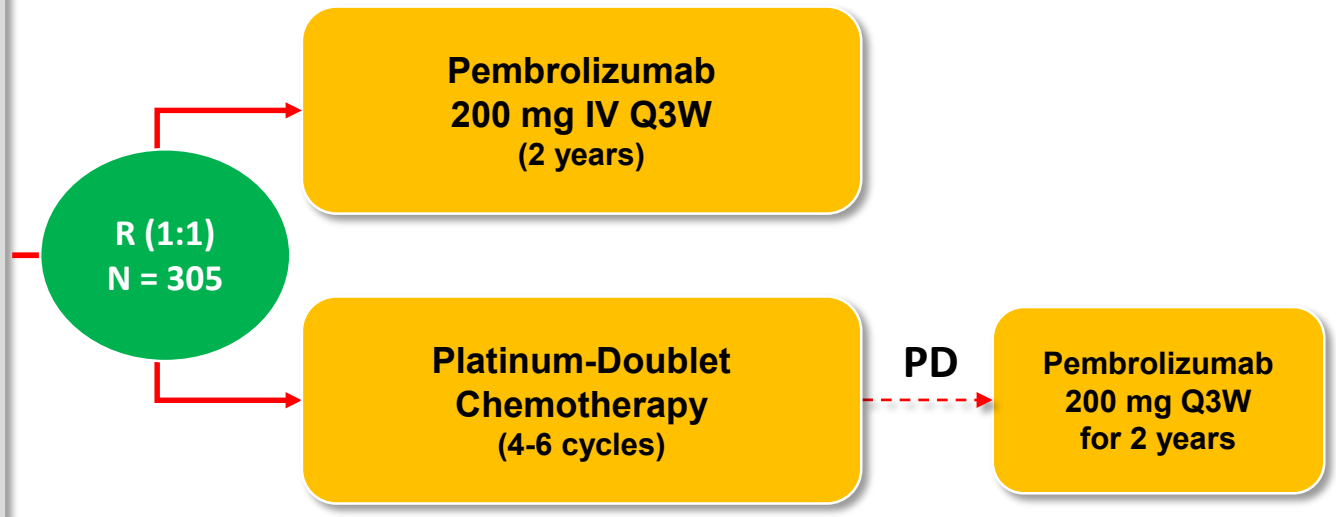
Reck M et al, ASCO 2020.

KEYNOTE-024: Pembrolizumab vs. Chemotherapy for PD-L1 Positive (≥ 50%)

NSCLC Study Design (NCT021427389)

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

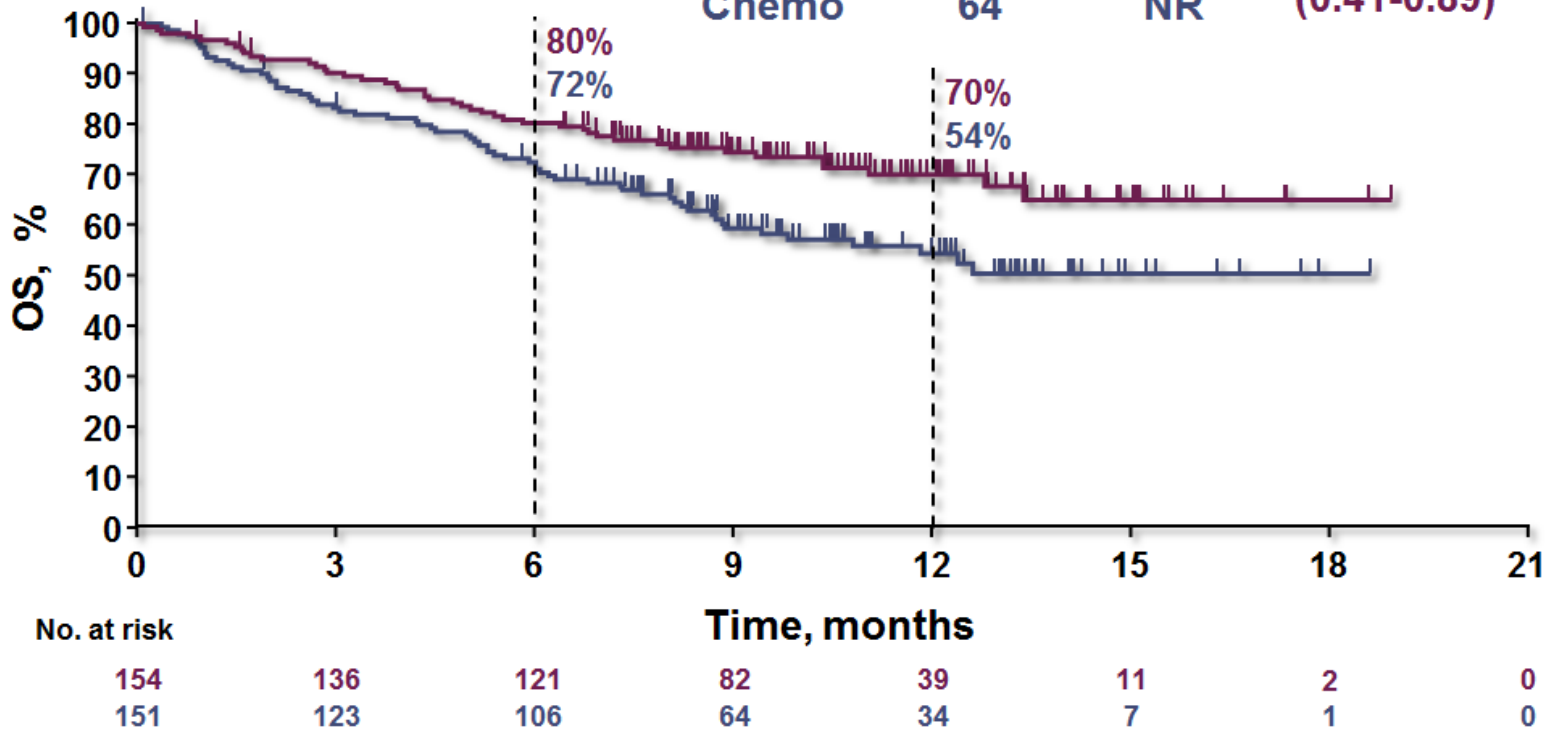


Reck M et al, ESMO 2016, NEJM 2016

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

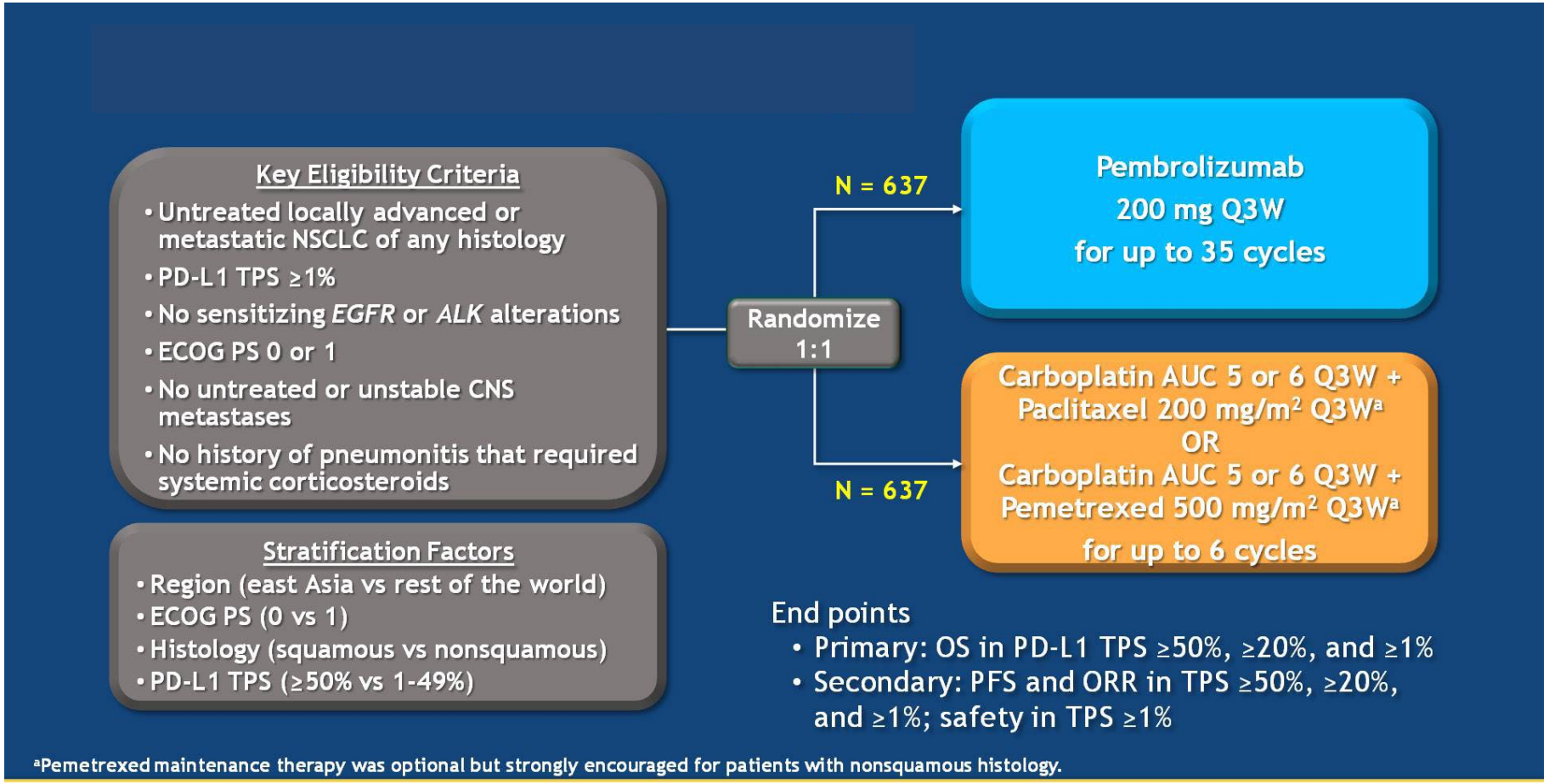
Overall Survival

	Events, n	Median, mo	HR (95% CI)	*P*
Pembro	44	NR	0.60 (0.41-0.89)	0.005
Chemo	64	NR		



Reck M et al, ESMO 2016, NEJM 2016

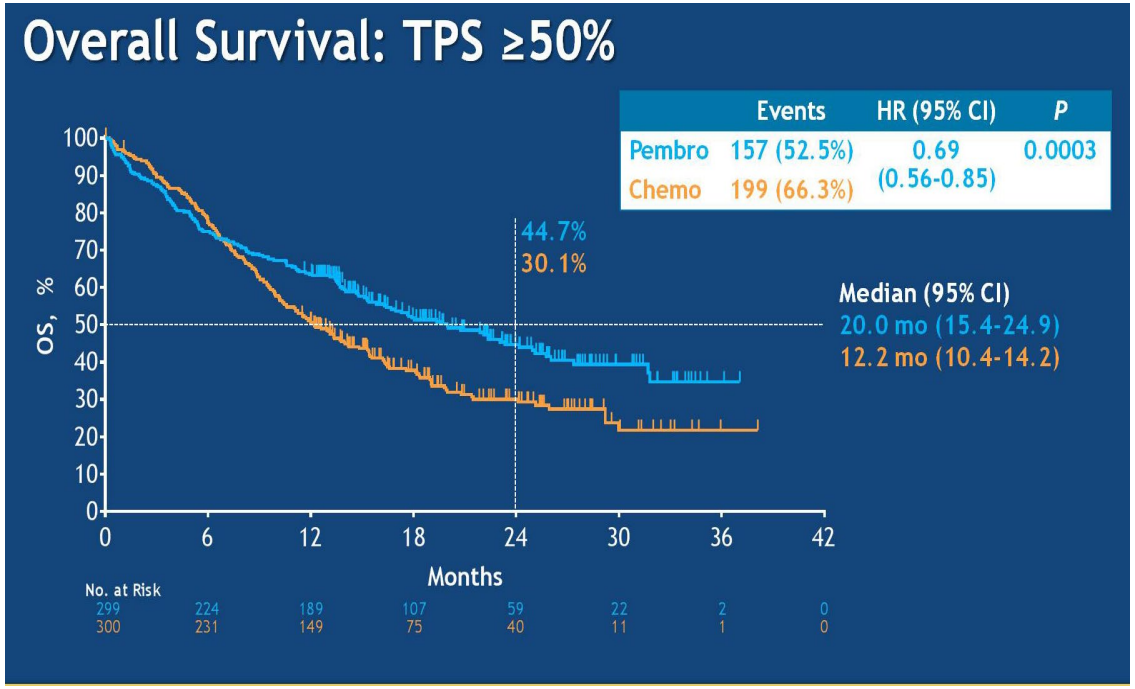
KEYNOTE-042: Pembrolizumab vs. Chemotherapy for PD-L1 ≥ 1% NSCLC

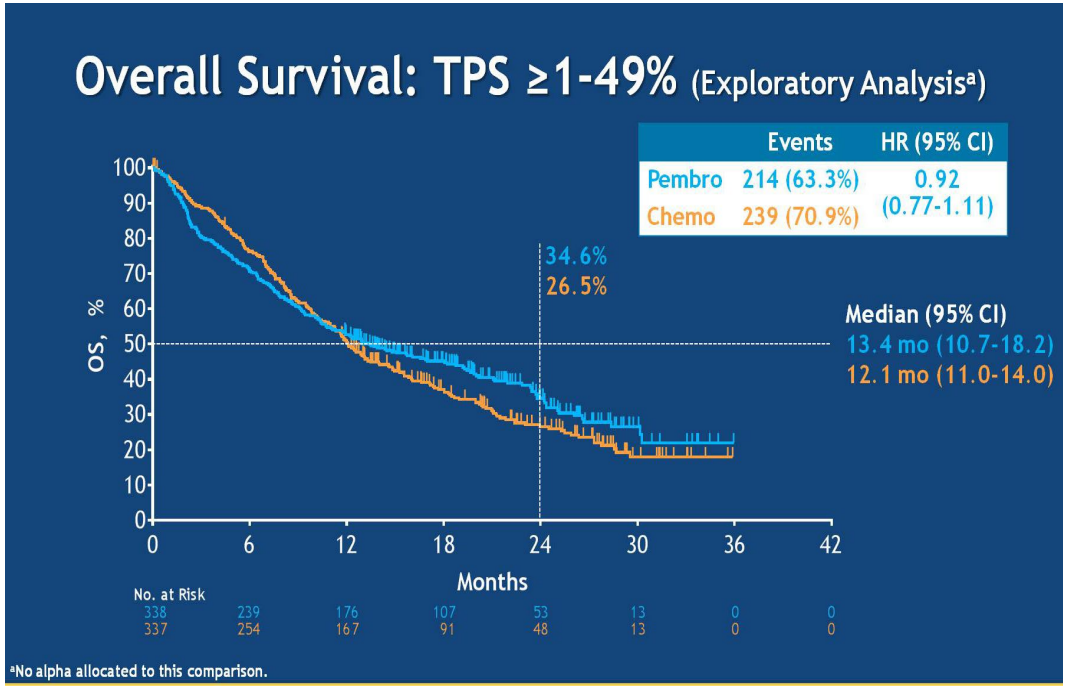


Lopes et al, ASCO 2018

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

Overall Survival

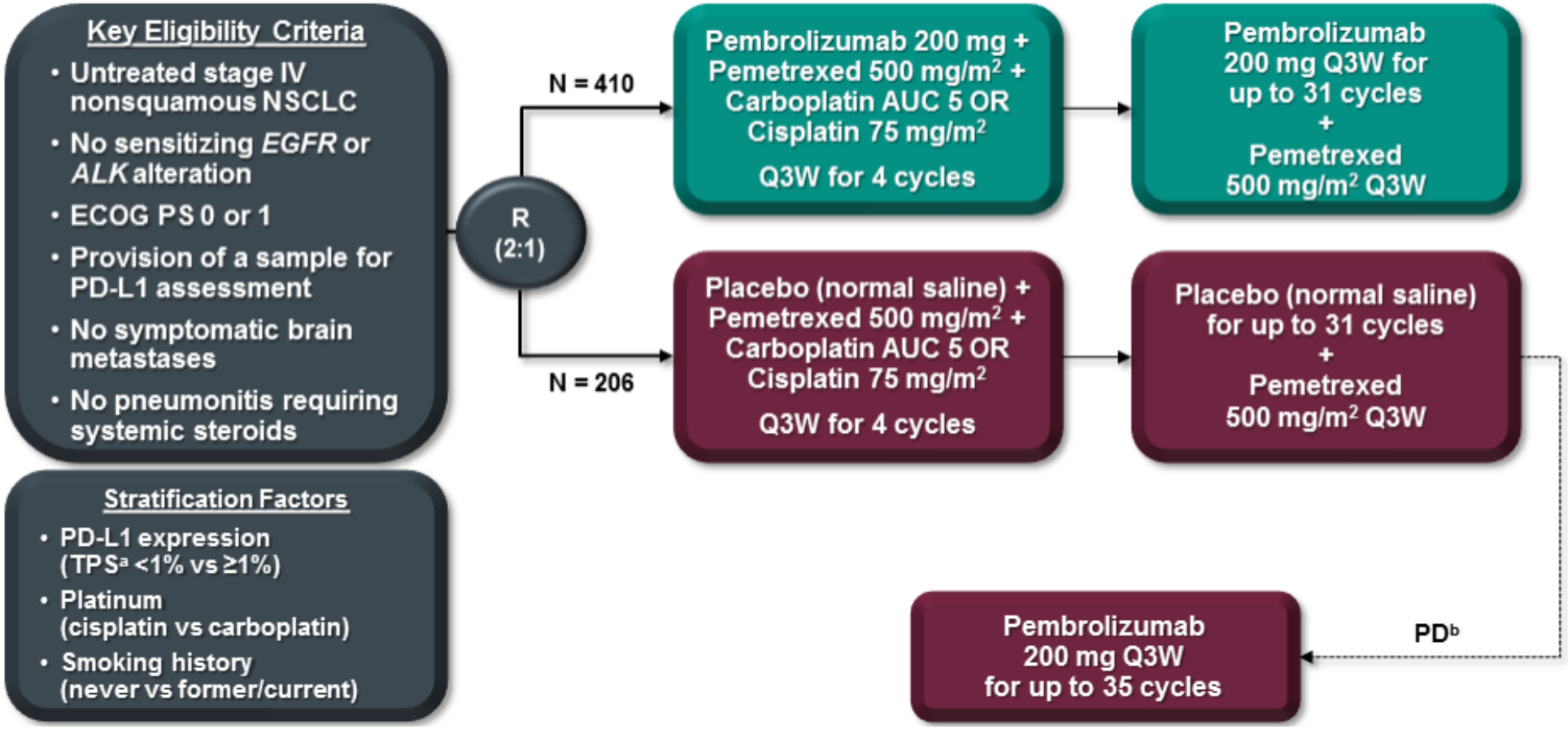




Survival benefit seemed to be driven by the TPS ≥ 50% subset with little benefit witnessed in the subset TPS = 1 - 49%

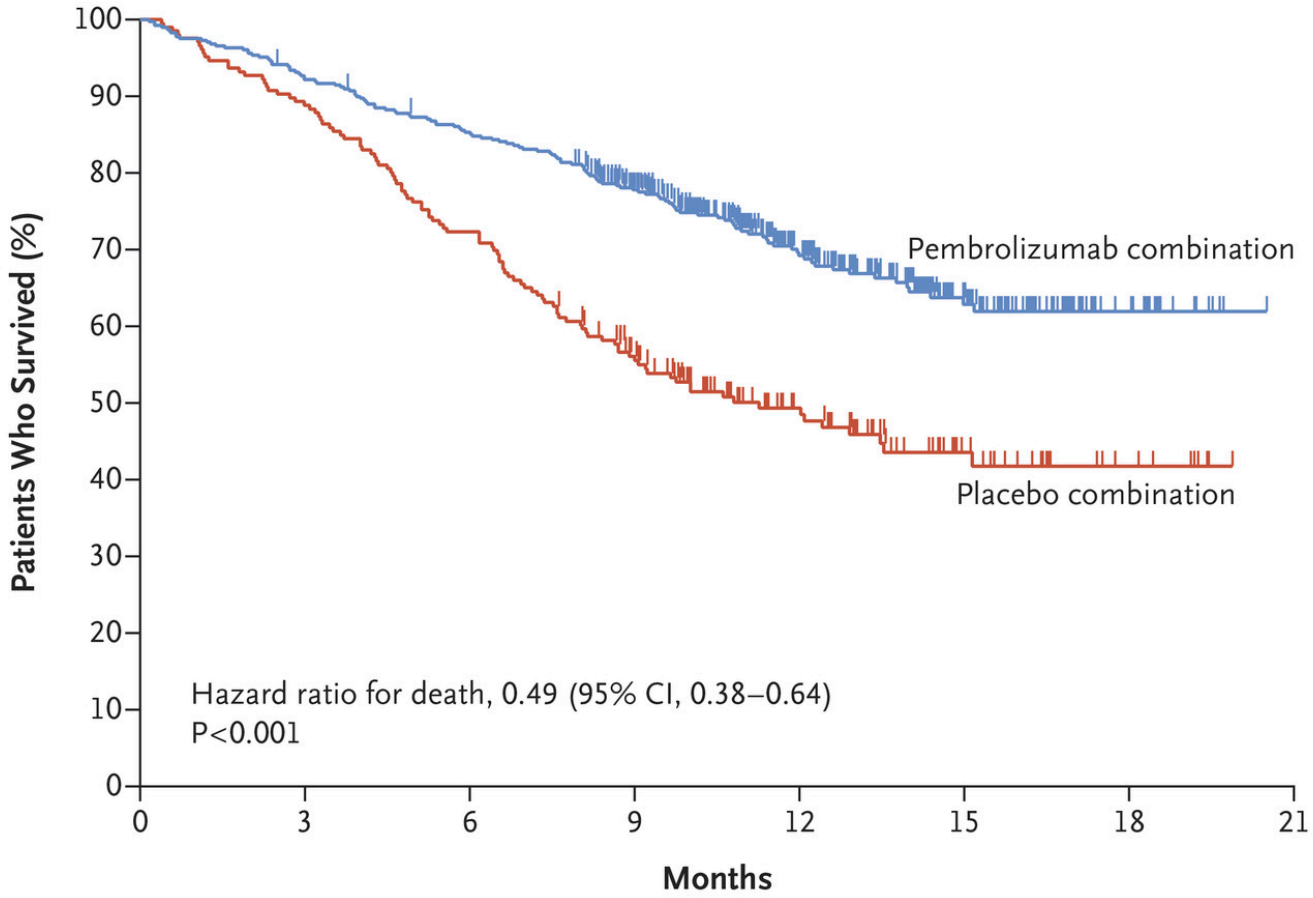
Lopes et al, ASCO 2018

KEYNOTE-189: Pembrolizumab/Platinum /Pemetrexed vs Chemotherapy Alone for Advanced Non-Squamous NSCLC



Ghandi et al, NEJM 2018

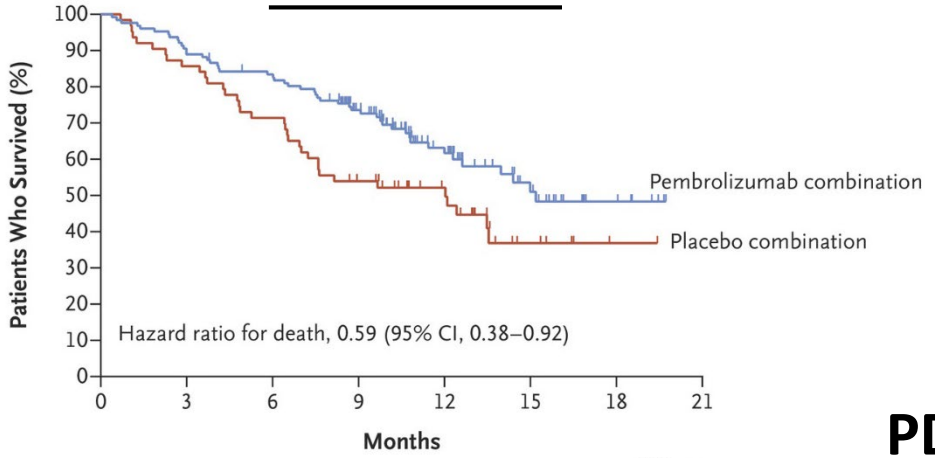
KEYNOTE-189: Pembrolizumab/Platinum /Pemetrexed vs Chemotherapy Alone for Advanced Non-Squamous NSCLC



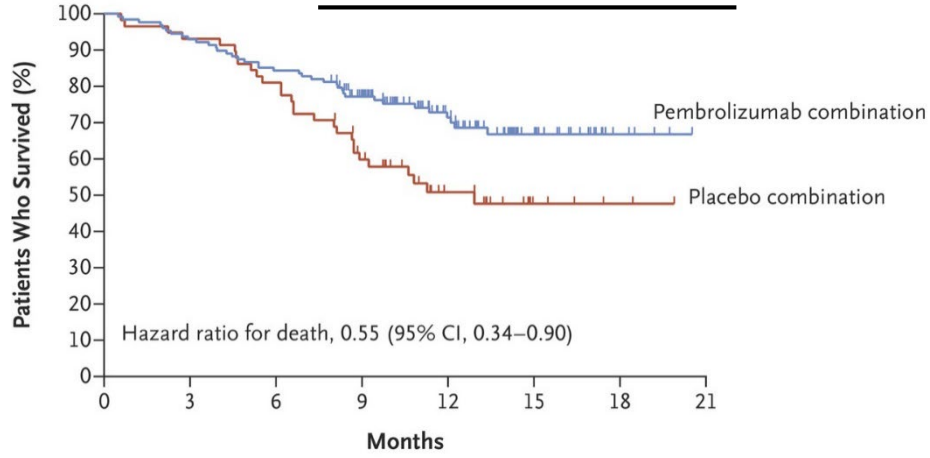
Ghandi et al, NEJM 2018

KEYNOTE-189: Pembrolizumab/Platinum /Pemetrexed vs Chemotherapy Alone for Advanced Non-Squamous NSCLC

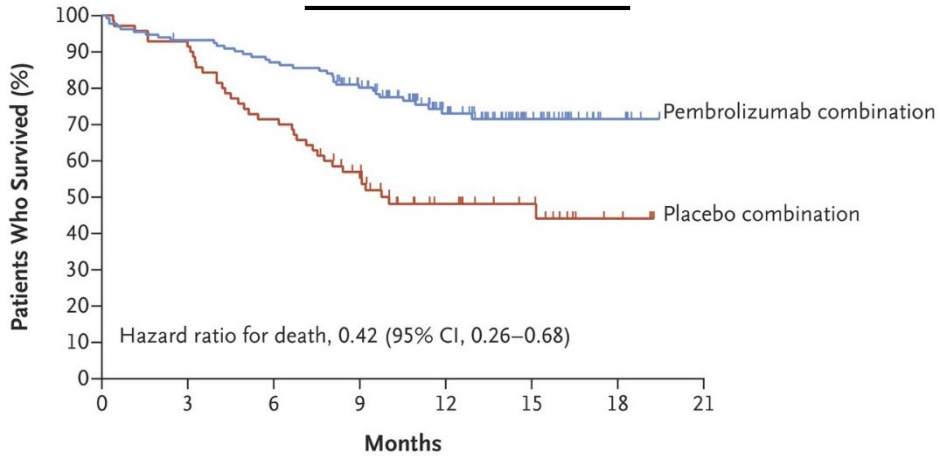
PD-L1 < 1%



PD-L1 = 1 – 49%

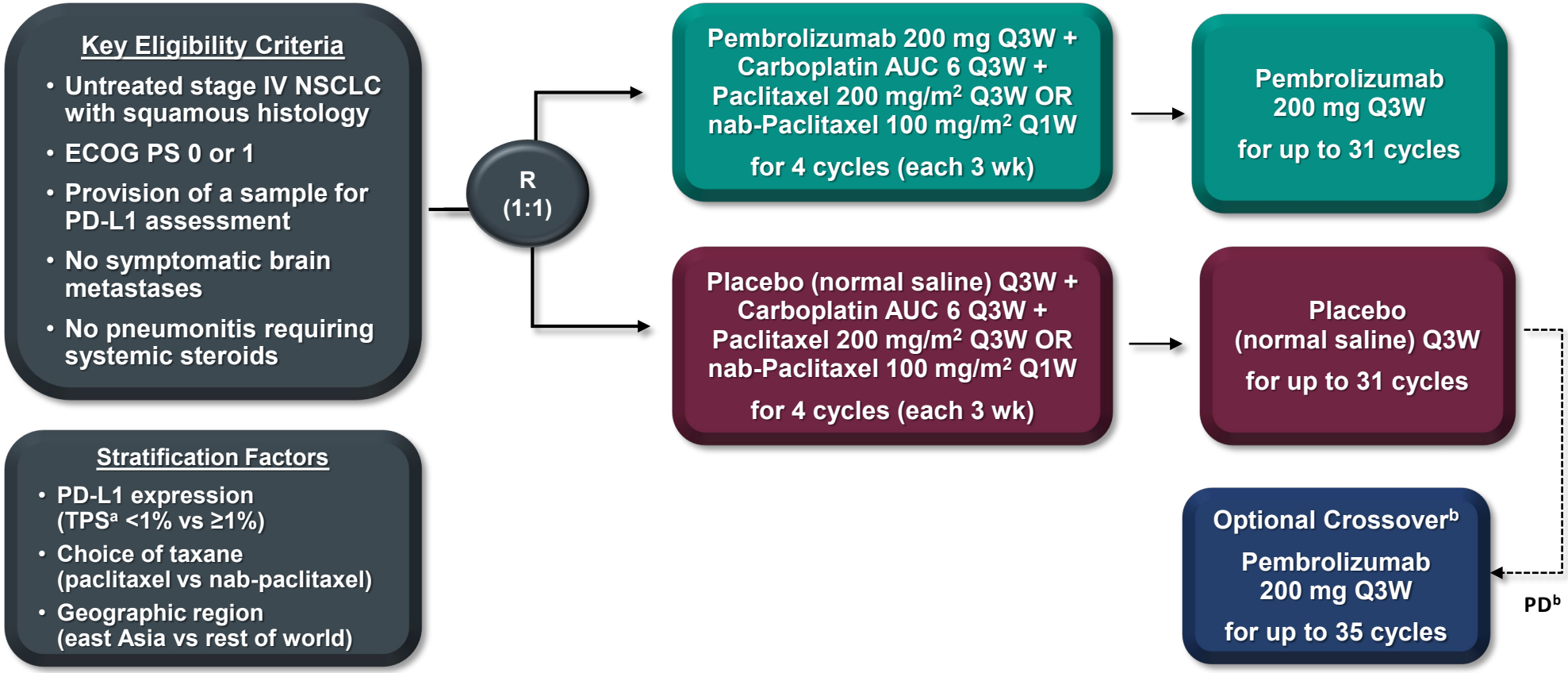


PD-L1 ≥ 50%



Ghandi et al, NEJM 2018

KEYNOTE-407: Pembrolizumab/Chemotherapy vs Chemotherapy Alone for Advanced Squamous-Cell NSCLC

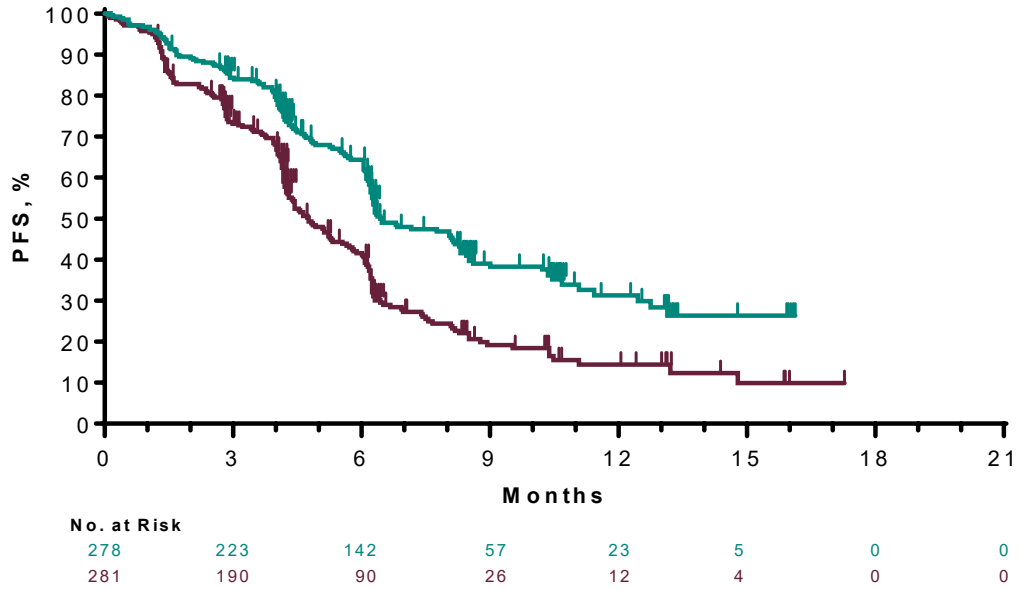


Paz-Ares et al, ASCO 2018

KEYNOTE-407: Pembrolizumab/Chemotherapy vs Chemotherapy Alone for Advanced Squamous-Cell NSCLC

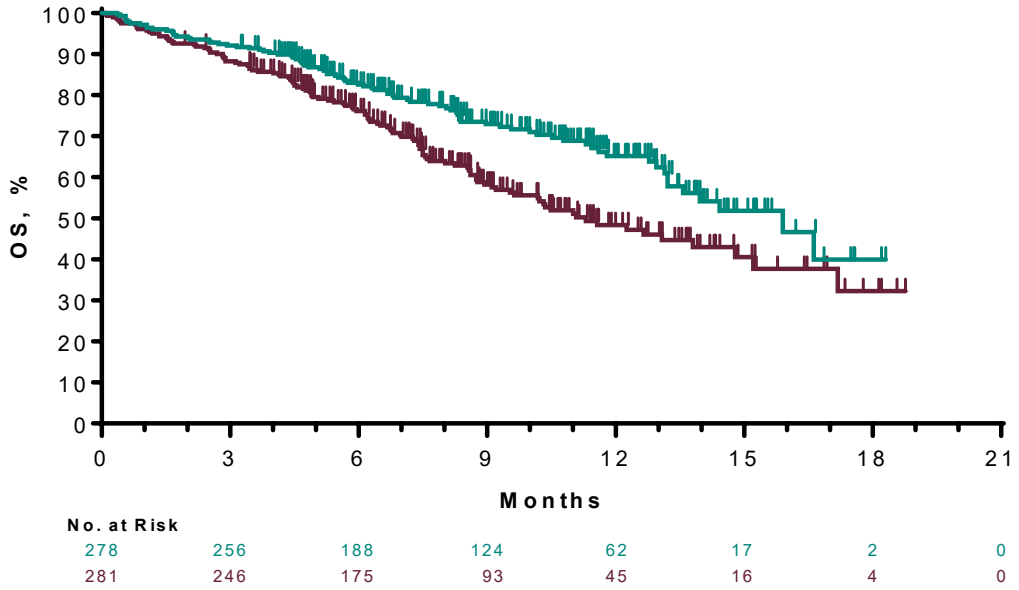
PFS (RECISTv1.1, BICR)

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



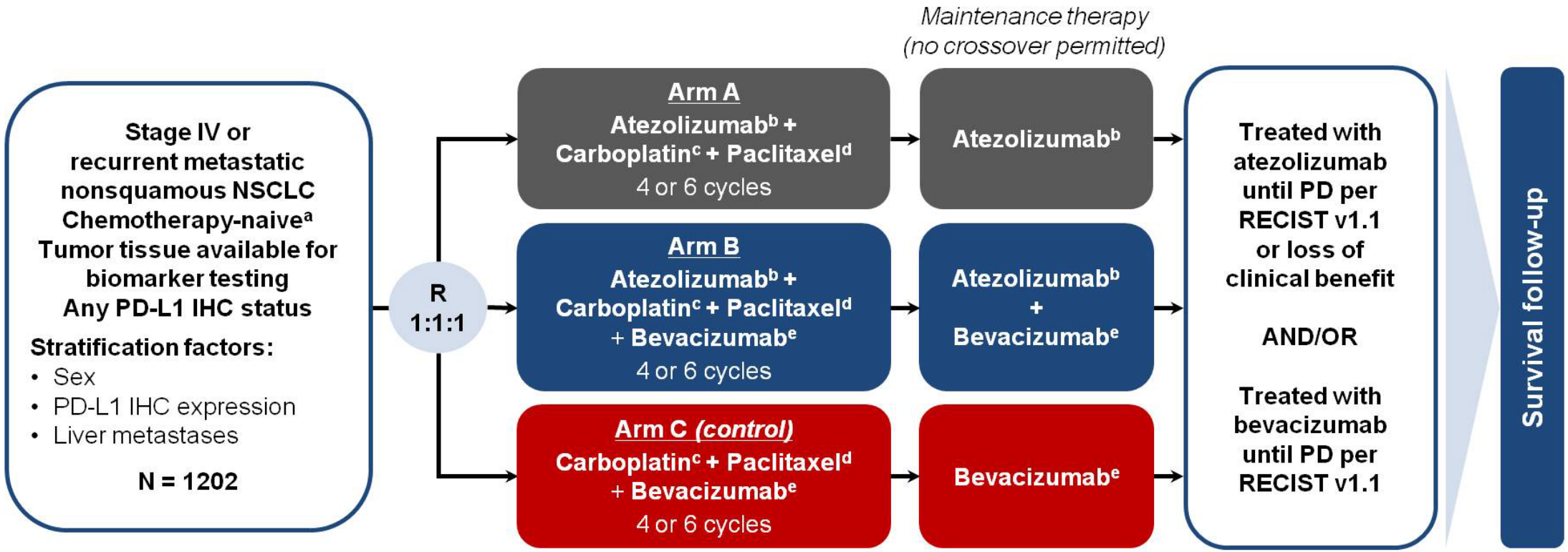
Overall Survival

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



Paz-Ares et al, ASCO 2018

IMPOWER 150: Atezolizumab/Carboplatin/ Paclitaxel/Bevacizumab vs Carboplatin/Paclitaxel/ Bevacizumab in Advanced Non-Squamous NSCLC

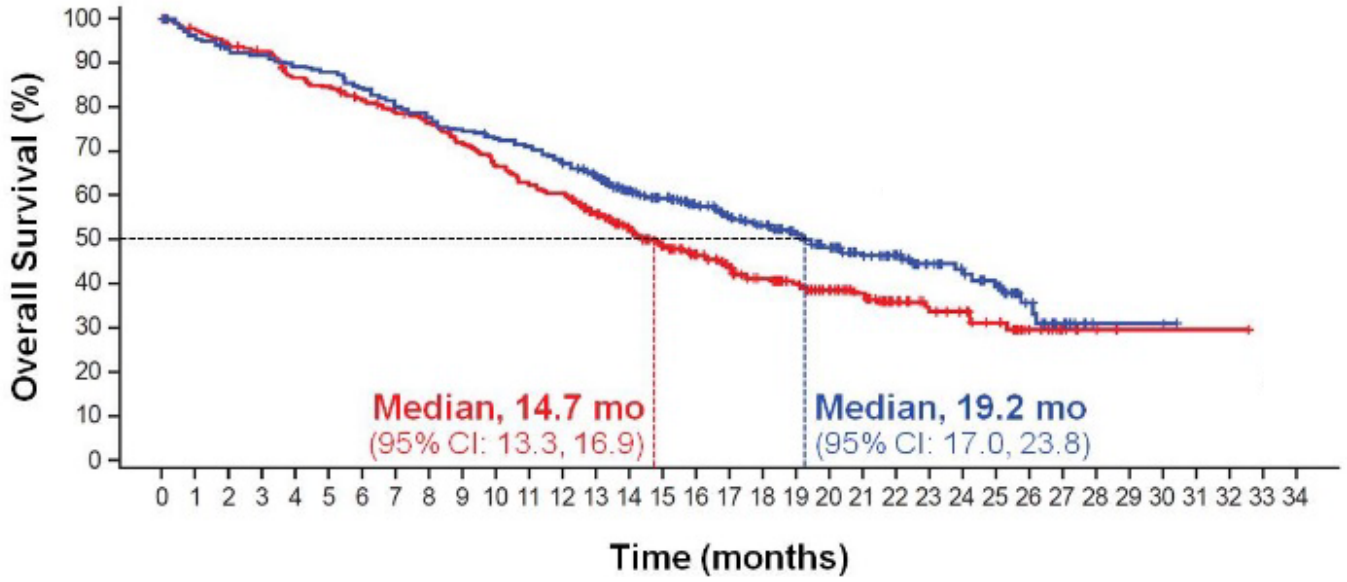


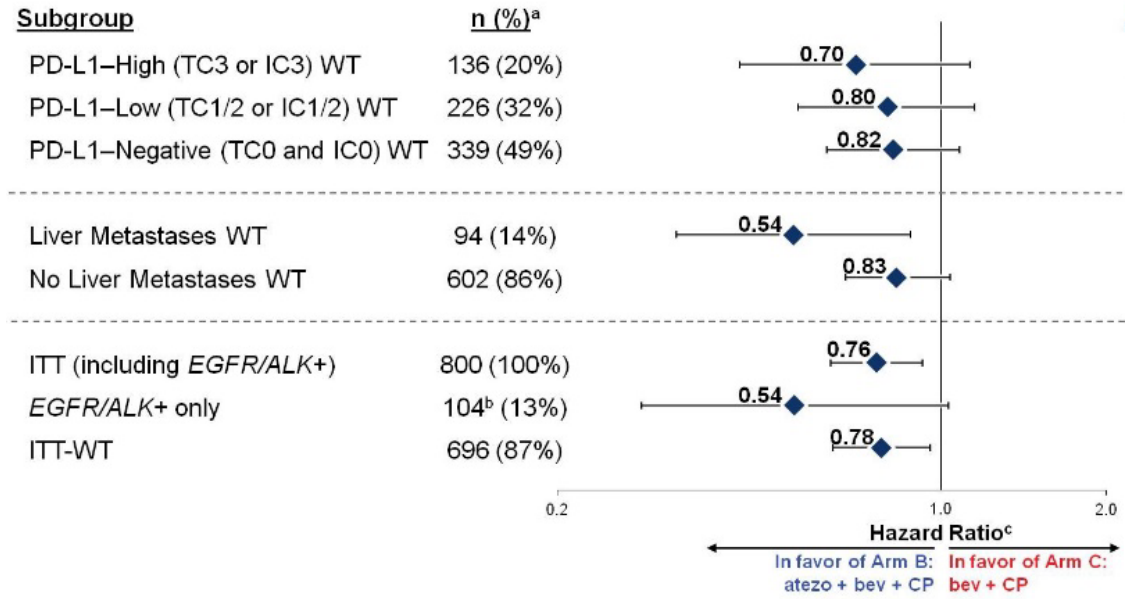
Socinski et al, NEJM 2018

IMPOWER 150: Atezolizumab/Carboplatin/ Paclitaxel/Bevacizumab vs Carboplatin/Paclitaxel/ Bevacizumab in Advanced Non-Squamous NSCLC

Landmark OS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
12-month	67%	61%
18-month	53%	41%
24-month	43%	34%

HR[a], 0.78
(95% CI: 0.64, 0.96)
***P* = 0.0164**
Median follow-up: ~20 mo

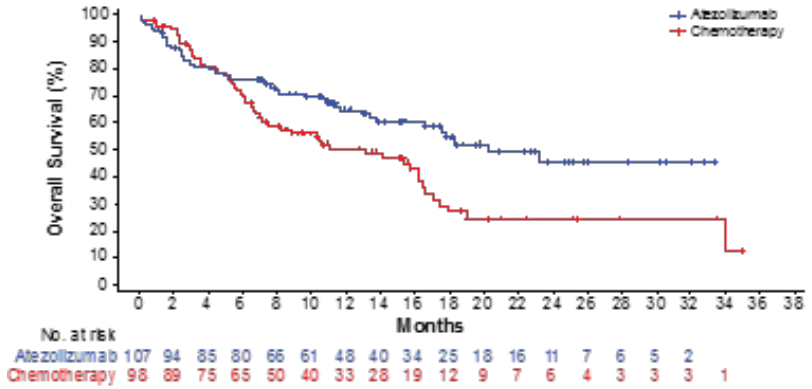




Socinski et al, NEJM 2018

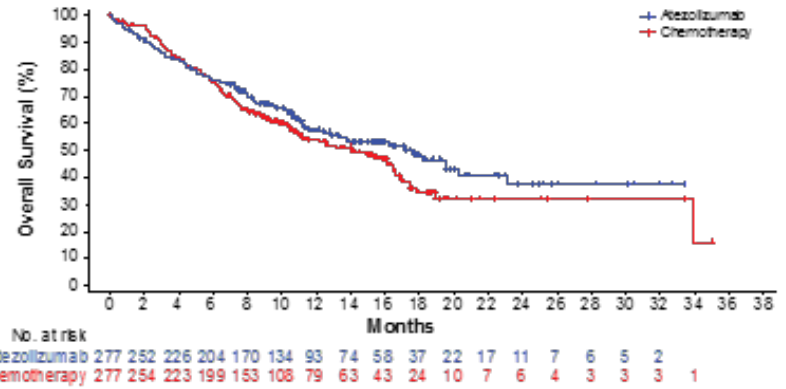
IMpower110: Atezolizumab vs chemotherapy in 1L NSCLC

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]

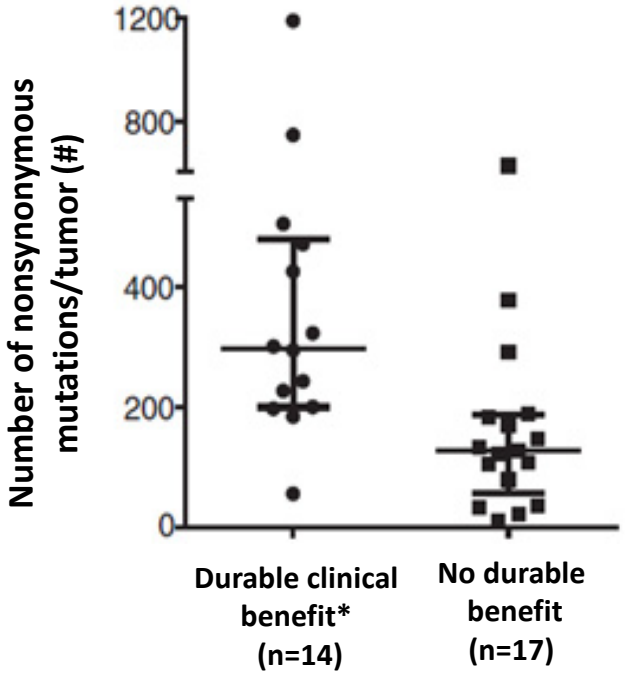


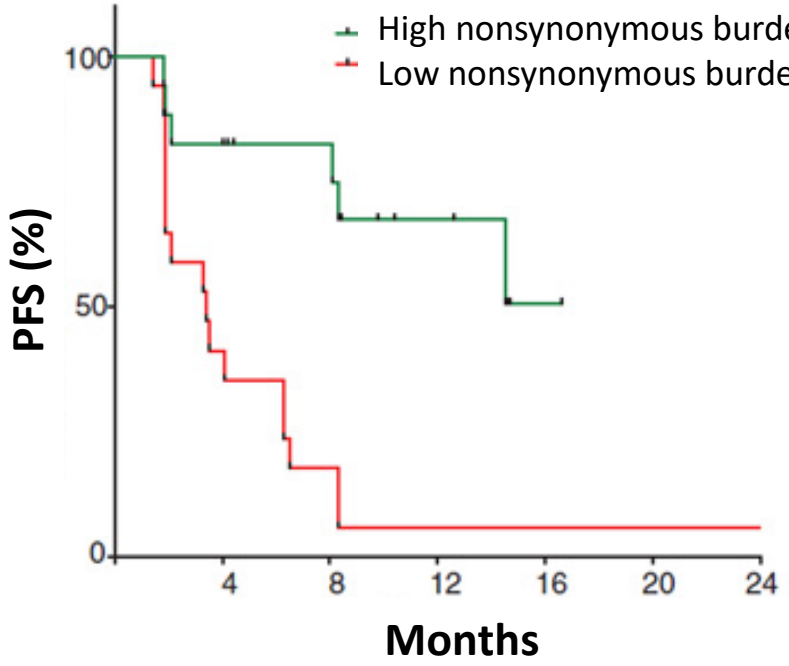
	Atezo (n = 277)	Chemo (n = 277)
mOS, mo	17.5	14.1
HR[b] (95% CI)	0.83 (0.65, 1.07)	

Herbst, ESMO-IO 2019.

Tumor Mutational Burden (TMB) may Determine Sensitivity to PD-1 Blockade in NSCLC

In two independent cohorts, higher nonsynonymous tumor mutational burden (TMB) was associated with improved objective response, durable clinical benefit, and PFS.

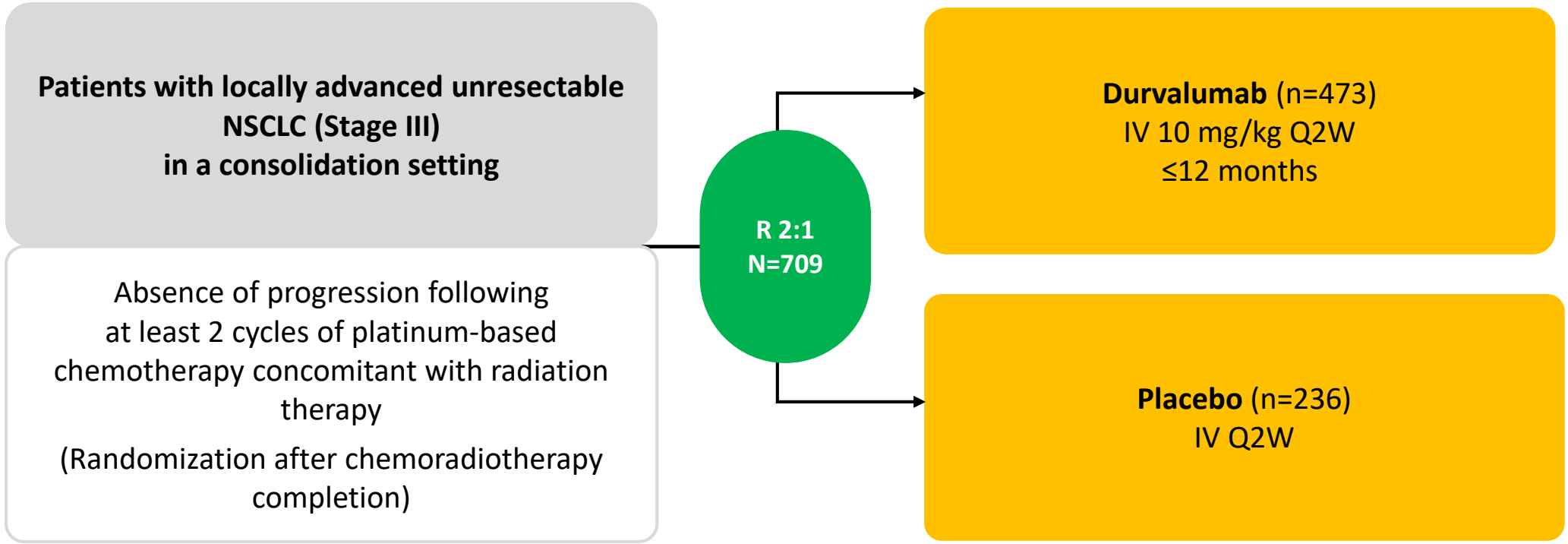




***Partial or stable response lasting > 6 mo**

Rizvi N et al, Science, 2015

PACIFIC (NCT02125461): Durvalumab after chemoradiotherapy in Stage III NSCLC

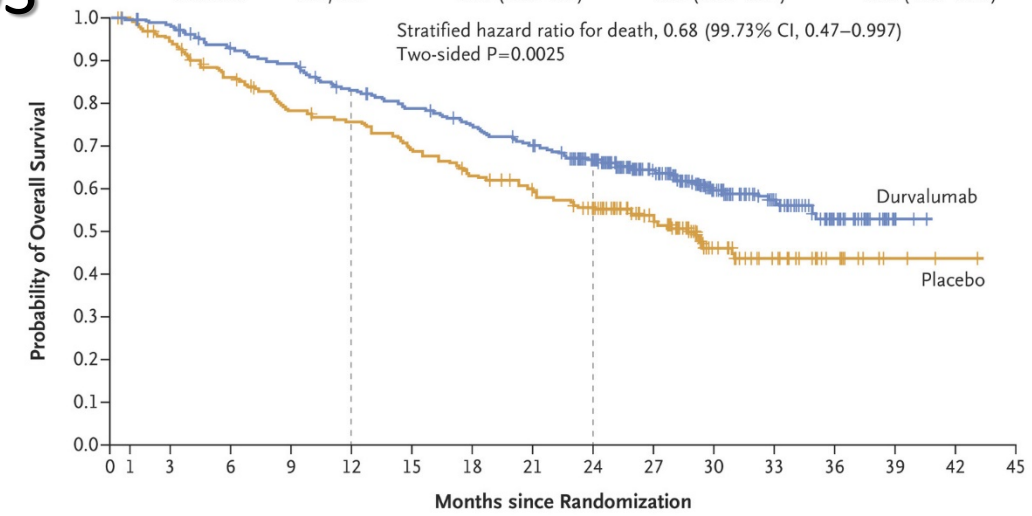


Antonia et al, NEJM 2018

PACIFIC (NCT02125461): Durvalumab after chemoradiotherapy in Stage III NSCLC

OS

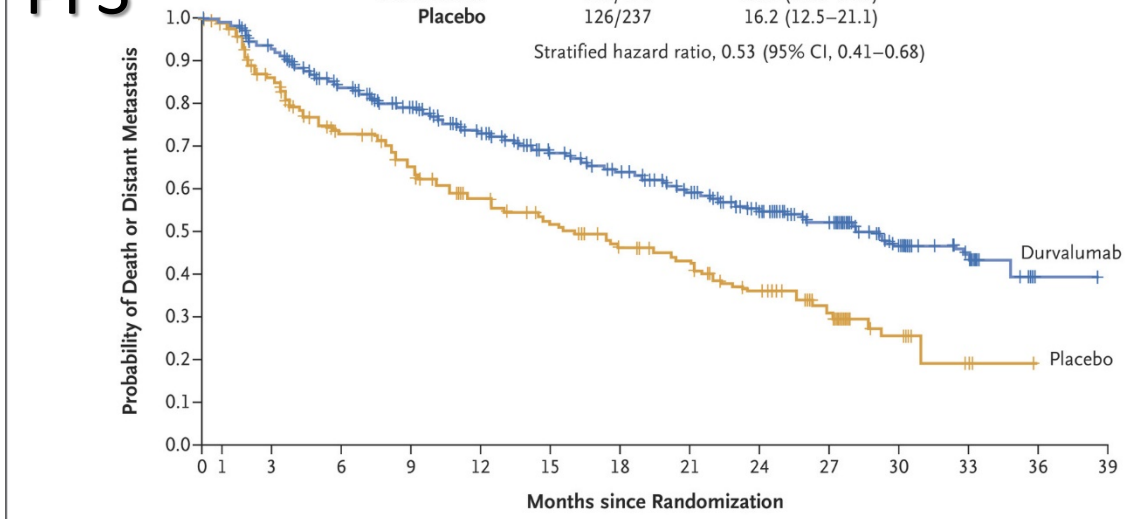
	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



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 Time to Death or Distant Metastasis (95% CI)
		mo
Durvalumab	182/476	28.3 (24.0–34.9)
Placebo	126/237	16.2 (12.5–21.1)

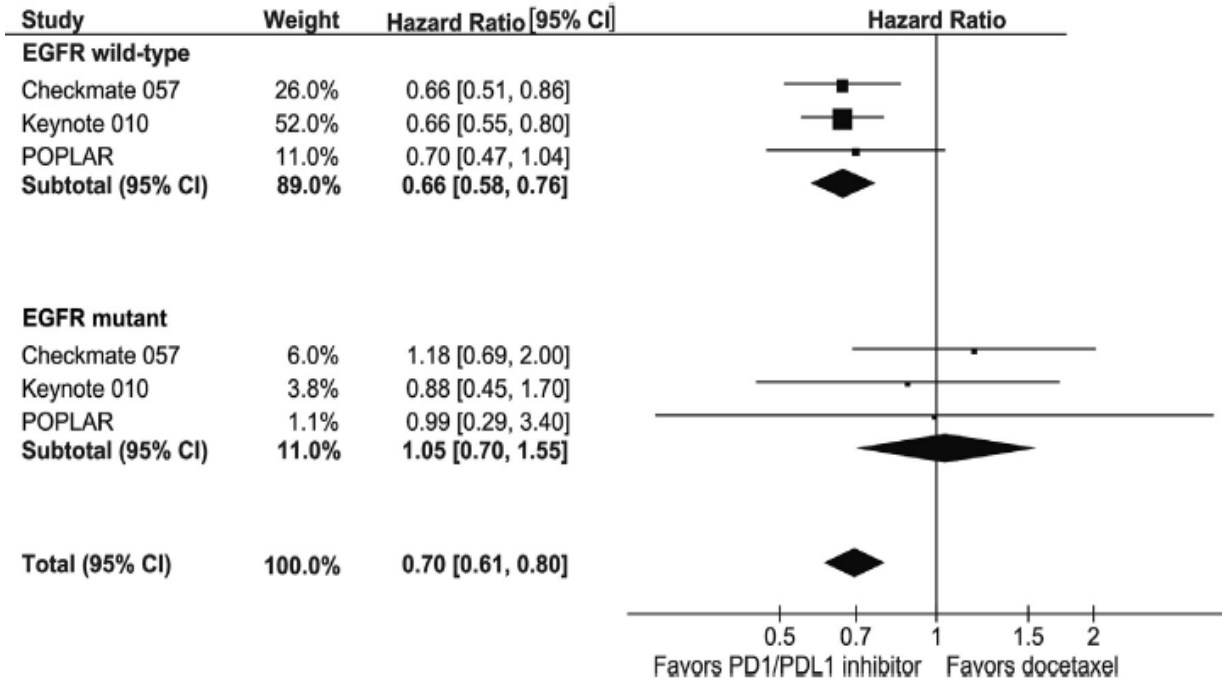


No. at Risk														
Durvalumab	476	419	357	316	259	223	194	163	129	92	46	25	1	0
Placebo	237	189	139	118	95	77	64	54	39	27	12	5	0	0

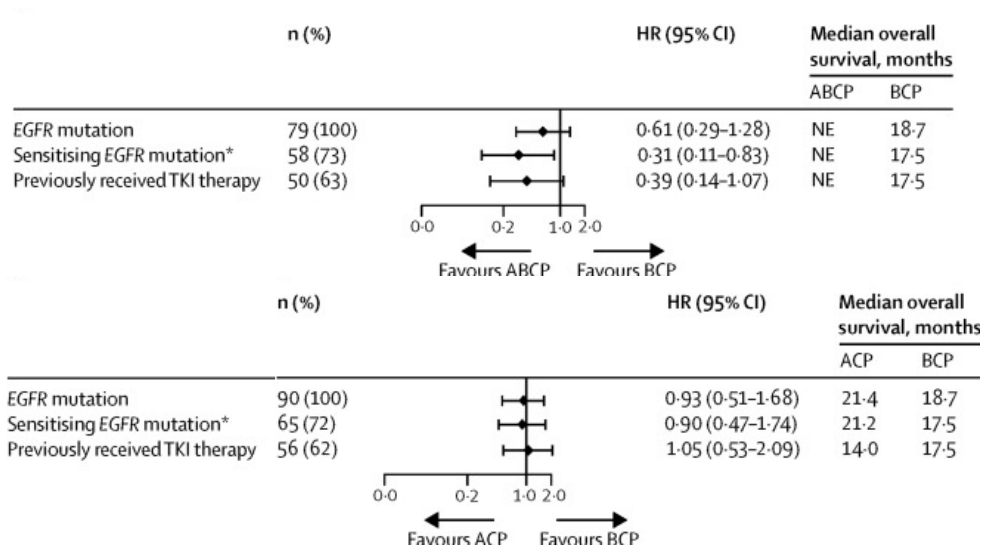
Antonia et al, NEJM 2018

Checkpoint Inhibitors in Metastatic EGFR-Mutated NSCLC

Meta-Analysis: CM-057, KN-010, POPLAR; IMPOWER-150



IMPOWER-150



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

PD-1/PD-L1 Inhibitors Increase *Overall Survival* in 2L Advanced NSCLC

CHECKMATE 017 (nivolumab)

	Median Overall Survival *mo (95% CI)*	1-Yr Overall Survival *% of patients (95% CI)*	No. of Deaths
Nivolumab (N–135)	9.2 (7.3–13.3)	42 (34–50)	86
Docetaxel (N–137)	6.0 (5.1–7.3)	24 (17–31)	113

CHECKMATE 057 (nivolumab)

	Nivolumab (n = 292)	Docetaxel (n = 290)
mOS, mo	12.2	9.4

HR = 0.73 (96% CI: 0.59, 0.89); *P* = 0.0015

KEYNOTE 010 (TPS ≥ 1%) (pembrolizumab)

Treatment Arm	Median (95% CI), mo	HR* (95% CI)	P
Pembro 2 mg/kg	14.9 (10.4-NR)	0.54 (0.38-0.77)	0.0002
Pembro 10 mg/kg	17.3 (11.8-NR)	0.50 (0.36-0.70)	<0.0001
Docetaxel	8.2 (6.4-10.7)	--	--

OAK (atezolizumab)

HR, 0.73[a]
(95% CI, 0.62, 0.87)
P = 0.0003

Minimum follow up = 19 months

Brahmer NEJM 2015
Borghaei, NEJM 2015
Herbst Lancet 2016
Rittmeyer Lancet 2017

Small cell lung cancer

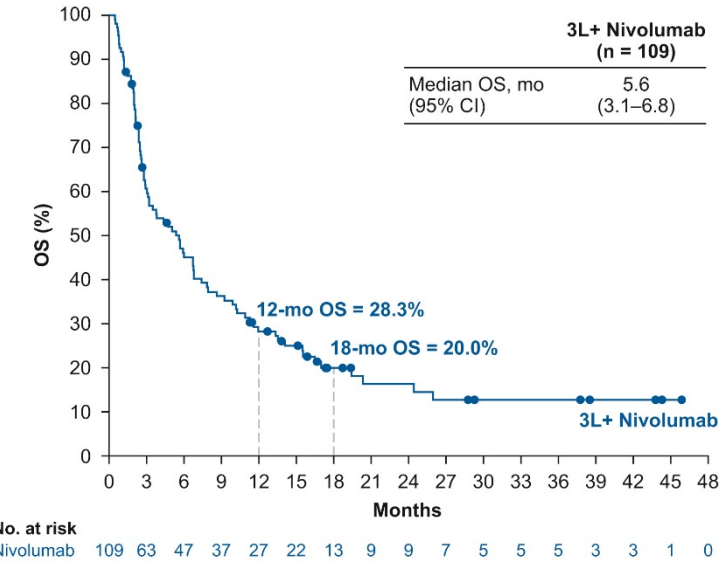
- 10-15% of lung cancers
- Almost exclusively former/current smokers
- Median survival 1-2 years after diagnosis
- Until recently, only one FDA-approved 2nd line option: topotecan – DOR: 3.3 months
- Recent approvals of immunotherapies mark the first progress in decades

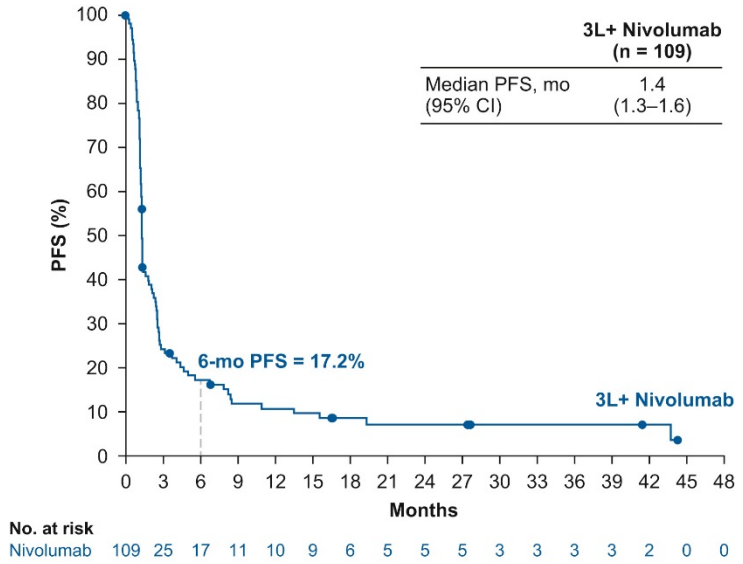
Approved checkpoint inhibitors in SCLC

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

CheckMate-032: Nivolumab in 3rd line SCLC

- Nivolumab in SCLC with progression on platinum chemotherapy and another therapy
- Nivolumab 3 mg/kg Q2W
- @28.3 months:
  - ORR: 11.9%
  - mDOR: 17.9 months

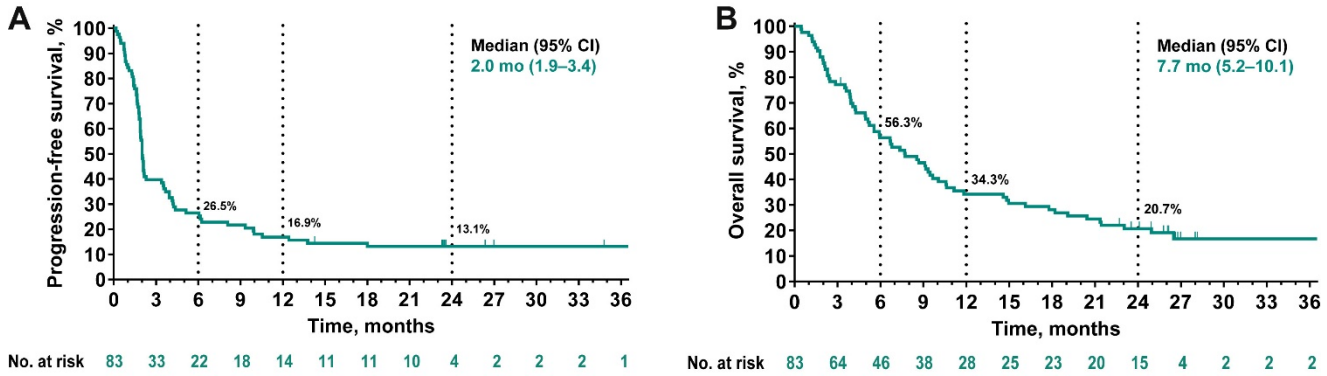




Ready, J Thorac Oncol 2019

Pembrolizumab in 3rd-line SCLC

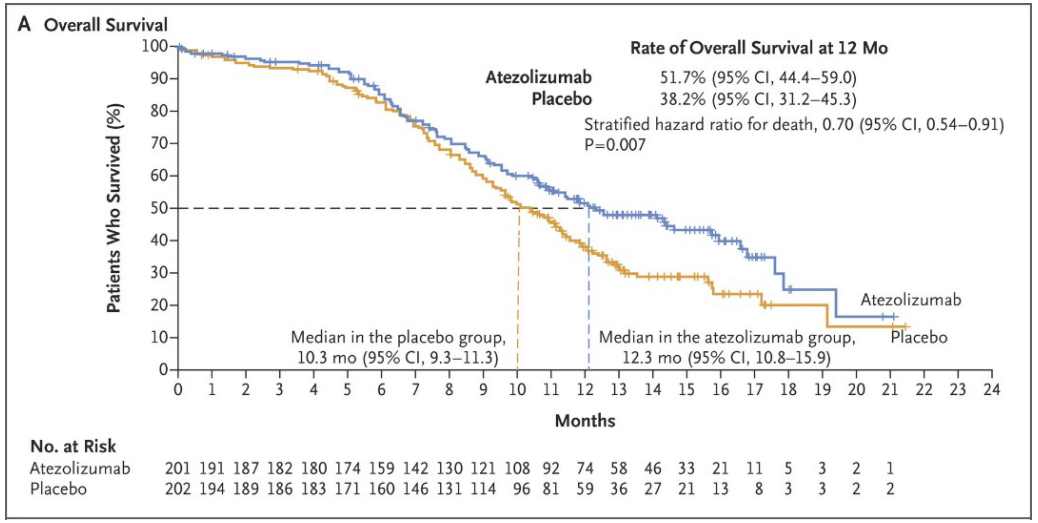
- KEYNOTE-028: PD-L1+ only (Cohort C1)
- KEYNOTE-158: PD-L1 +/- (Cohort G)
- Combined analysis:
- ORR: 19.3%
  - 2 CR, 14 PR
  - 14/16 responders were PD-L1+
  - 9/16 responders had response ≥18 mo.
- mOS: 7.7 months



Chung, J Thor Oncol 2020
Ott, J Clin Oncol 2017.

IMpower133: Atezolizumab + chemo in 1st-line SCLC

- Induction phase: four 21-day cycles of carboplatin and etoposide + atezolizumab (1200 mg once per cycle) or placebo
- Maintenance phase: either atezolizumab or placebo
- @13.9 mo:
  - mOS = 12.3 vs 10.3 mo
  - mPFS = 5.2 vs 4.3 mo



Horn, NEJM 2018.

Conclusions

- Immune checkpoint inhibitors have transformed the care of some lung cancer patients– **better quality, longer life**
- Moving immunotherapy to the **frontline** is associated with better outcomes
- Immune checkpoint inhibitors are used in **many settings**:
  - Advanced stage *non-small-cell* AND *small cell* lung cancers
  - Locally advanced *non-small-cell* lung cancer
- Determining **optimal single vs. combination therapy regimens** remains a challenge– better biomarkers 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*]

sitc Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Case Studies

Case Study 1

Your patient is a 59 y/o gentleman with a 45 pack/year tobacco history presents with R-sided weakness and is ultimately diagnosed with adenocarcinoma of the lung with metastases to the brain and bone.

Following palliative brain radiotherapy for the symptomatic brain metastases, he presents to your clinic for systemic therapy counseling and planning.

Aside from tobacco use and HTN, he has no other medical problems. ECOG PS is 1.

Comprehensive tumor molecular profiling performed on a nodal aspirate shows the following: microsatellite- stable, tumor mutation burden (TMB)- 50 muts/mb, PD-L1 22C3 tumor proportion score (TPS) 50%, and KRAS G12C mutation amongst others.

Case Study 1

Which of the following is advised as an evidence-based palliative systemic therapy regimen in this patient's case?

A. Carboplatin/Pemetrexed
B. Carboplatin/Pemetrexed/Pembrolizumab
C. Pembrolizumab
D. B and C
E. All of the above

Case Study 1

Answer:

A. Carboplatin/Pemetrexed

B. Carboplatin/Pemetrexed/Pembrolizumab

C. Pembrolizumab

D. B and C

E. All of the above

Case Study 1

Discussion:

Notable aspects of this patient's case include the following:

59 y/o gentleman with a 45 pack/year tobacco history presents with adenocarcinoma of the lung with metastases to the brain and bone.

He has no other medical problems. ECOG PS is 1.

Comprehensive tumor molecular profiling shows: microsatellite- stable, tumor mutation burden (TMB)- 50 muts/mb, PD-L1 TPS 50%, and KRAS G12C mutation.

On the basis of the landmark KEYNOTE trials, either **Pembrolizumab** alone (**KEYNOTE-024**) OR combination chemoimmunotherapy with **Carboplatin/Pemetrexed/Pembrolizuma**b (**KEYNOTE-189**) is a reasonable FDA-approved regimen for this patient due to **high tumor PD-L1 (TPS ≥50%) and absence of other actionable genomic alterations**.

Given high likelihood of brisk response with less toxicity associated with single agent Pembrolizumab vs. combination chemoimmunotherapy, **Pembrolizumab alone** is generally favored in this setting (high tumor PD-L1)– though whether upfront combination therapy might be superior in this setting remains uncertain.

Case Study 2

Six months into the treatment course, the patient develops a grade 3 colitis from Pembrolizumab.

He is admitted and treated with high dose IV steroids and remains on a slow outpatient PO steroid taper.

Most recent CT torso and MRI brain performed just prior to hospitalization shows overall partial response to therapy since initiation of Pembrolizumab 6 months ago; there are no new sites of disease/evidence of disease progression.

Case Study 2

What do you advise next for your patient?

A. Resume Pembrolizumab IV every 3 weeks.
B. Administer Pembrolizumab at extended intervals of IV every 6 weeks.
C. Switch to Carboplatin/Pemetrexed.
D. Transition to active surveillance for now.

Case Study 2

Answer:

A. Resume Pembrolizumab IV every 3 weeks.

B. Administer Pembrolizumab at extended intervals of IV every 6 weeks.

C. Switch to Carboplatin/Pemetrexed.

D. Transition to active surveillance for now.

Case Study 2

Discussion:

The patient has had a known, significant immune-related adverse event (colitis, grade 3).

Suspension of Pembrolizumab and treatment with high dose steroids, followed by steroid taper over a minimum of 4-6 weeks is advised.

Re-challenge with Pembrolizumab might be considered in future following detailed discussion of risks, benefits, and alternatives with the patient.

Immune-related adverse events may be accompanied by continued durable disease control even in the absence of continued regular administration of the immune checkpoint inhibitor.

Active surveillance is a safe and viable strategy if the overall disease burden is stable.