Immunotherapy for the Treatment of Lung Cancer

Ticiana A. Leal, MD
Assistant Professor of Medicine
Thoracic Oncology Program Director
University of Wisconsin Carbone Cancer Center

Disclosures

- I will be discussing non-FDA approved indications during my presentation.
- Consulting Fees: Takeda, Novocure, AstraZeneca, Genentech, Inivata, Merck, PharmaMar, EMD Serono

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			Female		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All sites	321,670		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%

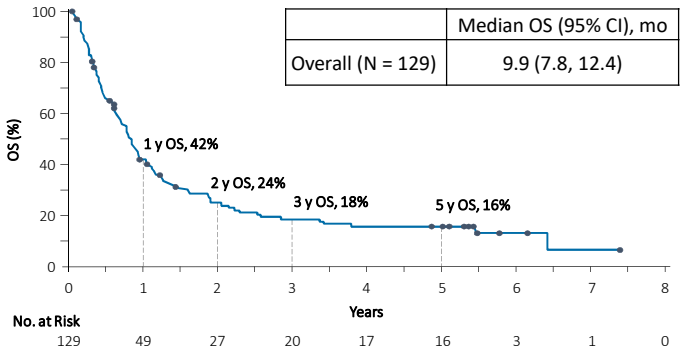
CA209-003: Nivolumab in Heavily-pretreated Advanced NSCLC (NCT00730639)

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

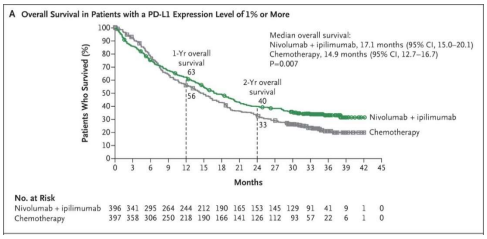
	Median OS (95% CI), mo
Overall (N = 129)	9.9 (7.8, 12.4)

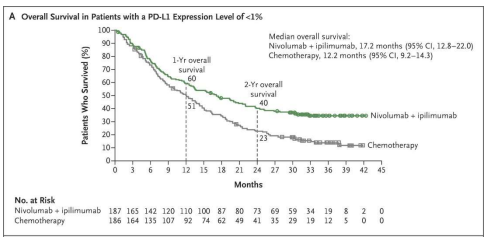


Gettinger et al. JCO 2018
Brahmer et al, AACR 2017
NCI SEER data, Lung and Bronchus Cancer, 2014

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

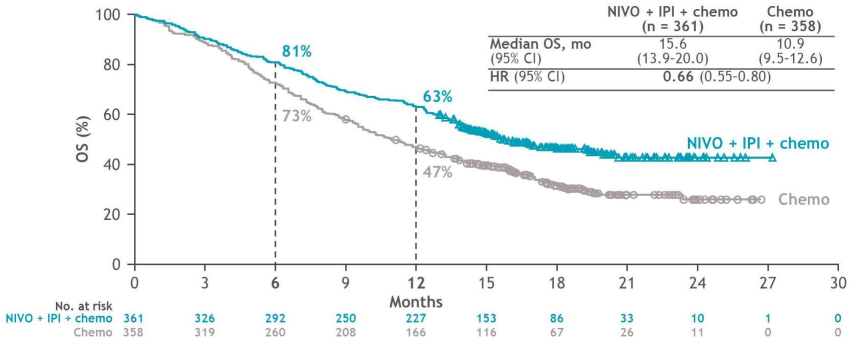
Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

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)

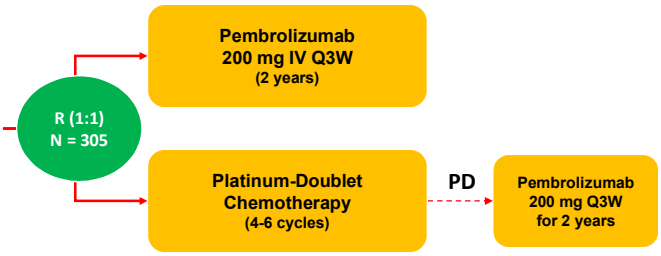
Reck M et al, ASCO 2020.

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

NSCLC Study Design (NCT021427389)

Key Eligibility Criteria

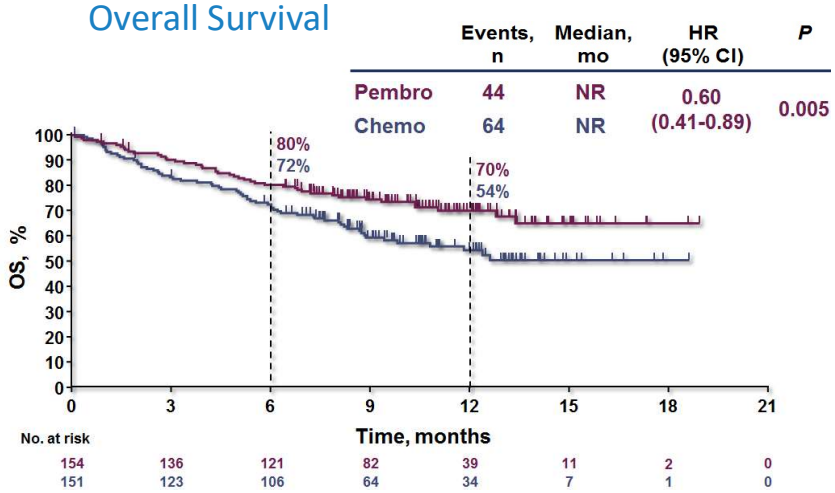
- ***Untreated*** stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No activating *EGFR* mutation or *ALK* translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy



Reck M et al, ESMO 2016, NEJM 2016

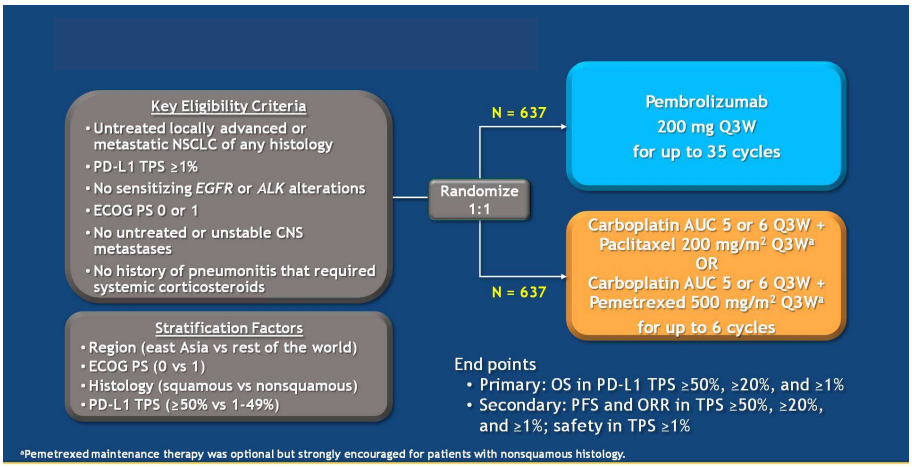
KEYNOTE-024: Pembrolizumab vs. Chemotherapy for PD-L1 ≥ 50% NSCLC

Overall Survival



Reck M et al, ESMO 2016, NEJM 2016

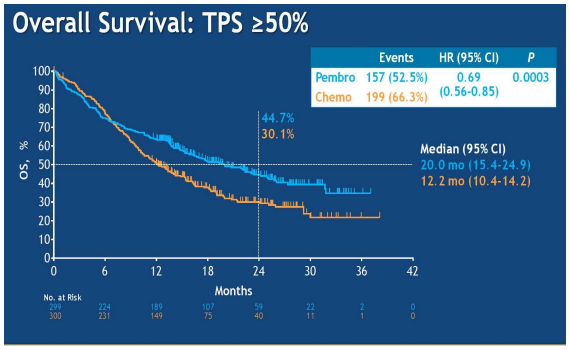
KEYNOTE-042: Pembrolizumab vs. Chemotherapy for PD-L1 ≥ 1% NSCLC

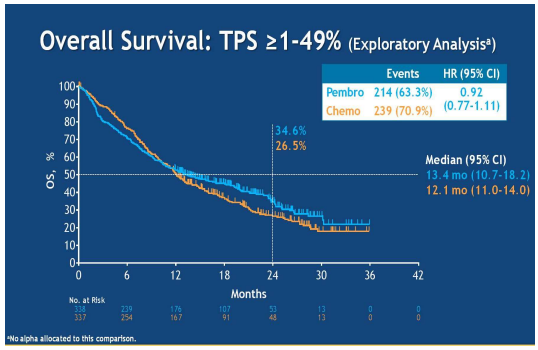


Lopes et al, ASCO 2018

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

Overall Survival

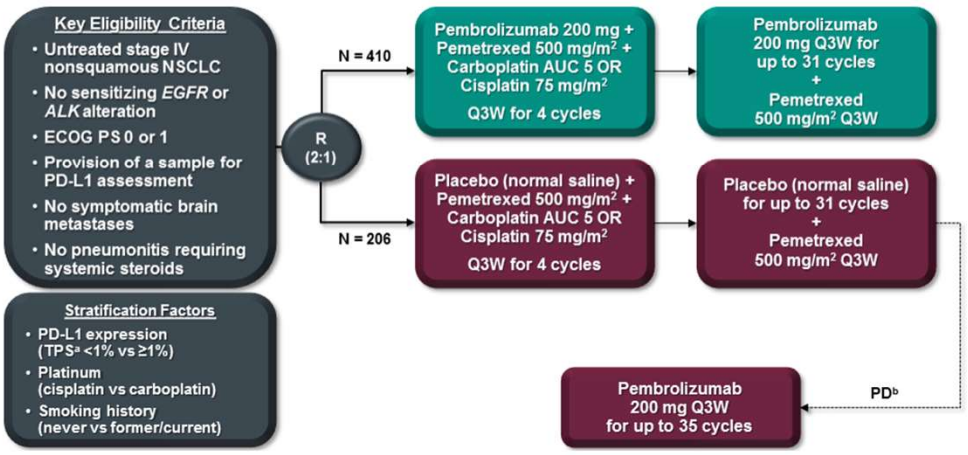




Survival benefit seemed to be driven by the TPS ≥ 50% subset with little benefit witnessed in the subset TPS = 1 - 49%

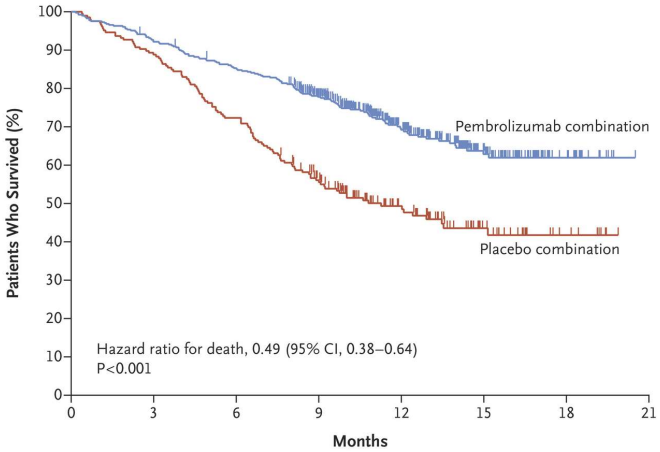
Lopes et al, ASCO 2018

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



Ghandi et al, NEJM 2018

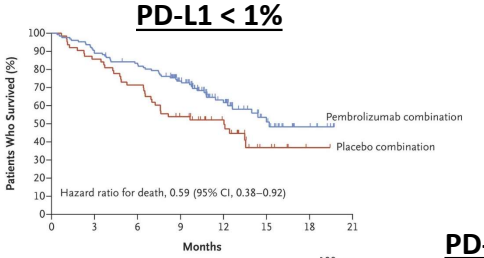
KEYNOTE-189: Pembrolizumab/Platinum /Pemetrexed vs Chemotherapy Alone for Advanced Non-Squamous NSCLC



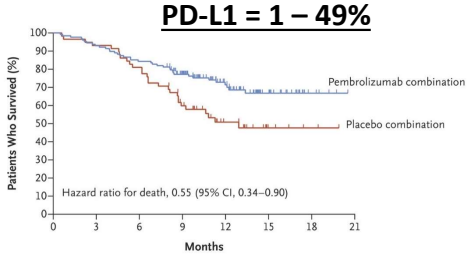
Ghandi et al, NEJM 2018

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

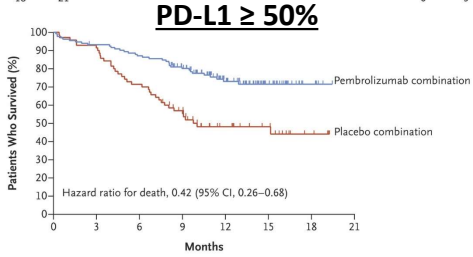
PD-L1 < 1%



PD-L1 = 1 – 49%

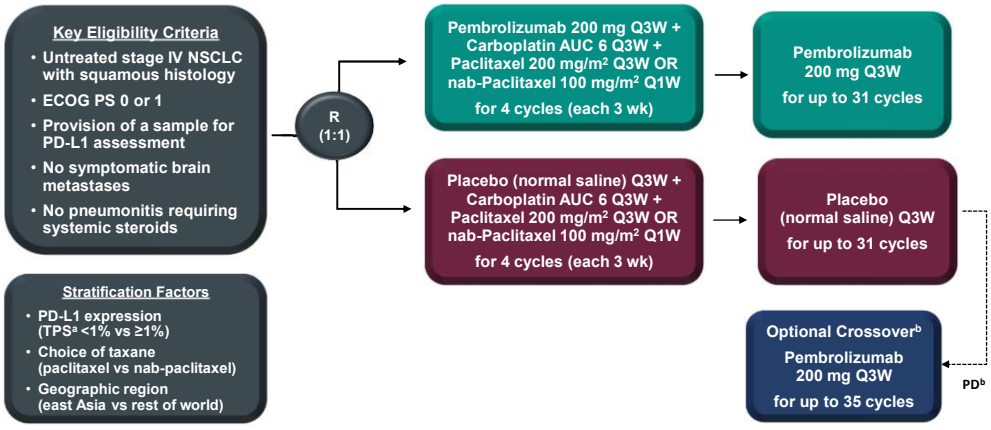


PD-L1 ≥ 50%



Ghandi et al, NEJM 2018

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

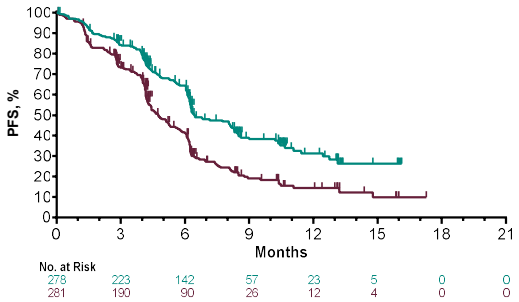


Paz-Ares et al, ASCO 2018

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

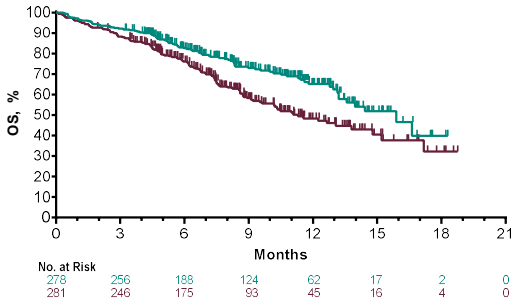
PFS (RECISTv1.1, BICR)

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



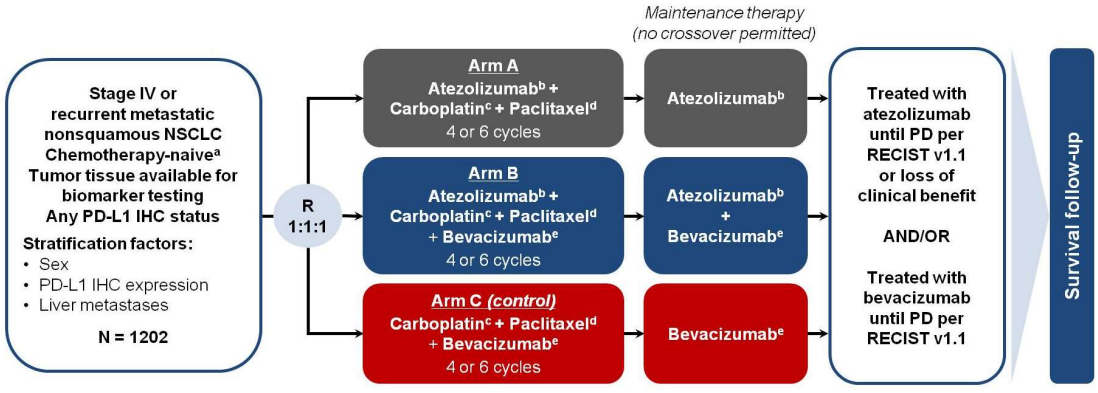
Overall Survival

	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

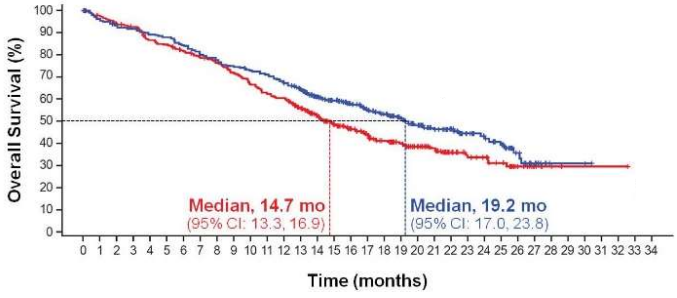


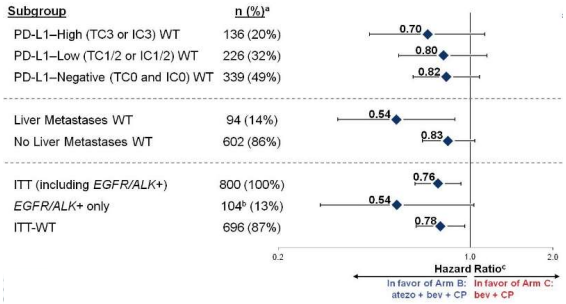
Socinski et al, NEJM 2018

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

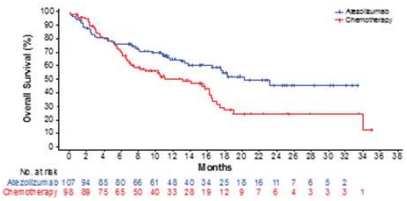




Socinski et al, NEJM 2018

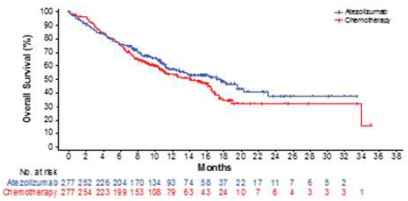
IMpower110: Atezolizumab vs chemotherapy in 1L NSCLC

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.

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

Patients with locally advanced unresectable NSCLC (Stage III) in a consolidation setting

Absence of progression following at least 2 cycles of platinum-based chemotherapy concomitant with radiation therapy

(Randomization after chemoradiotherapy completion)

R 2:1
N=709

Durvalumab (n=473)
IV 10 mg/kg Q2W
≤12 months

Placebo (n=236)
IV Q2W

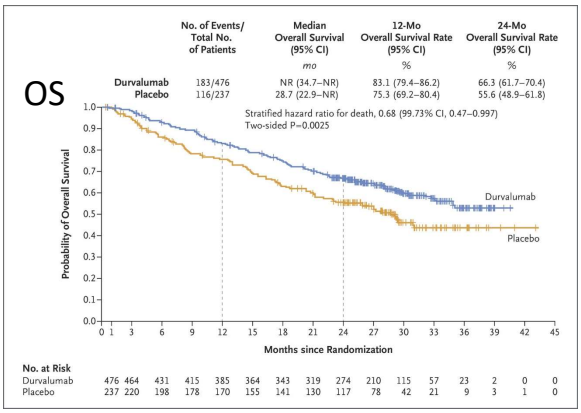
Antonia et al, NEJM 2018

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)

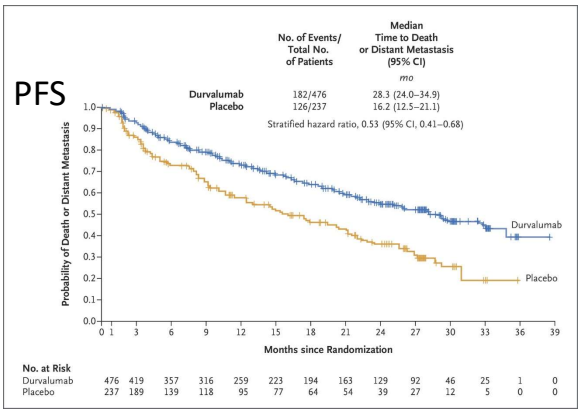
Stratified hazard ratio for death, 0.68 (99.73% CI, 0.47–0.997)
Two-sided P=0.0025



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)

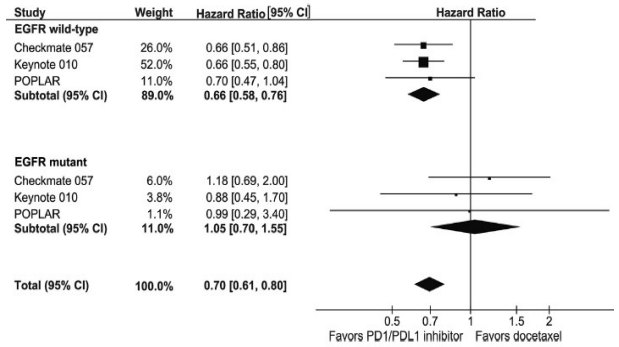
Stratified hazard ratio, 0.53 (95% CI, 0.41–0.68)

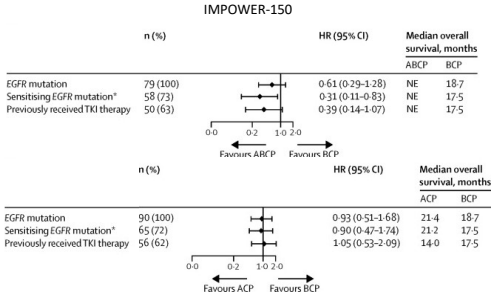


Antonia et al, NEJM 2018

Checkpoint Inhibitors in Metastatic EGFR-Mutated NSCLC

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

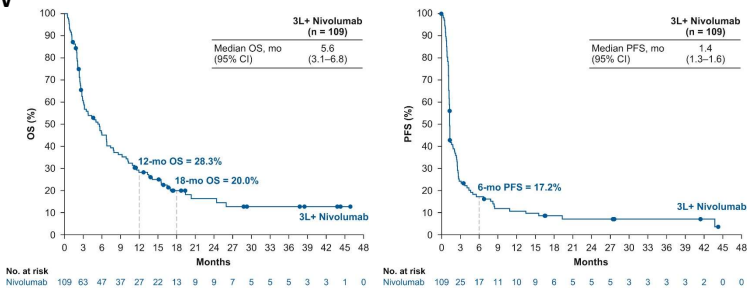
Slide 30

EE11 Dosing for last row:
Emily Ehlerding, 5/20/2020

EE12 For 4 cycles: 1500 mg durvalumab Q3W + chemotherapy;
Maintenance: 1500 mg durvalumab Q4W
Emily Ehlerding, 5/20/2020

CheckMate-032: Nivolumab in 3rd line SCLC

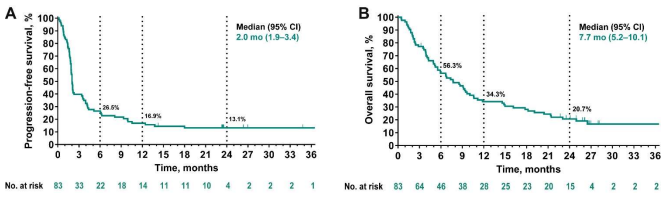
- Nivolumab in SCLC with progression on platinum chemotherapy and another therapy
- Nivolumab 3 mg/kg Q2W
- @28.3 months:
  - ORR: 11.9%
  - mDOR: 17.9 months



Ready, J Thorac Oncol 2019

Pembrolizumab in 3rd-line SCLC

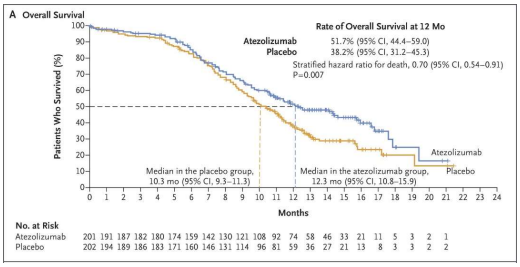
- KEYNOTE-028: PD-L1+ only (Cohort C1)
- KEYNOTE-158: PD-L1 +/- (Cohort G)
- Combined analysis:
- ORR: 19.3%
  - 2 CR, 14 PR
  - 14/16 responders were PD-L1+
  - 9/16 responders had response ≥18 mo.
- mOS: 7.7 months



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

IMpower133: Atezolizumab + chemo in 1st-line SCLC

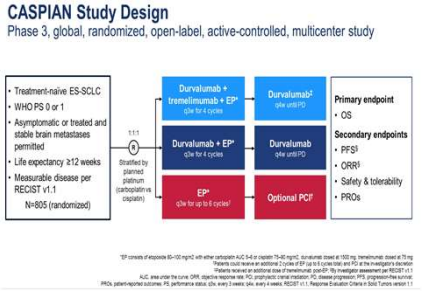
- Induction phase: four 21-day cycles of carboplatin and etoposide + atezolizumab (1200 mg once per cycle) or placebo
- Maintenance phase: either atezolizumab or placebo
- @13.9 mo:
  - mOS = 12.3 vs 10.3 mo
  - mPFS = 5.2 vs 4.3 mo

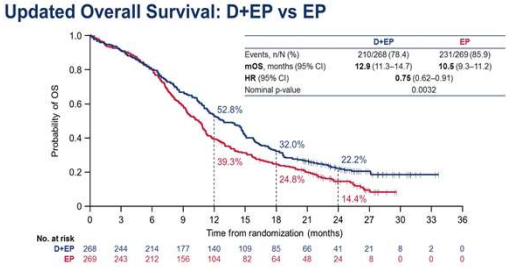


Horn, NEJM 2018.

CASPIAN: Durvalumab + chemo in 1st-line SCLC

- Induction phase: four 21-day cycles of carboplatin and etoposide + durvalumab or carboplatin and etoposide
- Maintenance phase: either durvalumab or observation



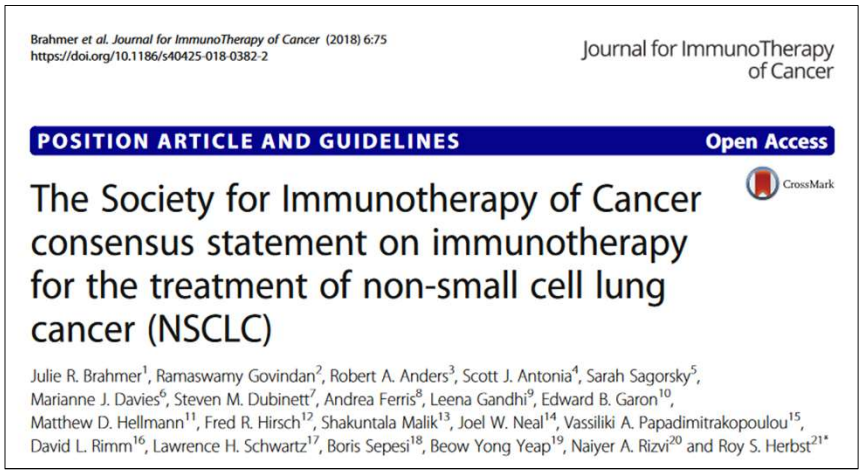


Paz-Ares, ASCO 2020.

Conclusions

- NSCLC has been a proving ground for checkpoint inhibitors
- Moving from 2nd/3rd line options to the front line
- Emerging biomarkers needed to refine patient selection, potential need for combination of biomarkers

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*]

Case Studies

Case Study 1

52 yo male with new diagnosis of adenocarcinoma of the right upper lobe with adrenal and liver metastases and ECOG PS 1 presents with mild cough and back pain. MRI of the brain was negative for metastatic disease. You order NGS on tumor tissue and PD-L1 is 60%. What would you do?

A) Start pembrolizumab.

B) Start carboplatin/pemetrexed/pembrolizumab.

C) Wait for NGS results prior to starting systemic therapy.

D) Start carboplatin/pemetrexed while waiting for the NGS results.

E) C or D.

Case Study 1

- NGS results show the following results:

- EGFR exon 19 deletion

- Patient received carboplatin/pemetrexed/pembrolizumab for 1 cycle. He tolerated the treatment well with mild adverse side effects of fatigue and mild anemia.

Case Study 1

- What is the best next step?

  A) Continue carboplatin/pemetrexed/pembrolizumab.
  B) Switch to osimertinib. Monitor closely for toxicities.
  C) Switch to carboplatin/pemetrexed and continue maintenance pemetrexed.
  D) Switch to erlotinib +/- ramucirumab.

Case Study 2

- 66 yo female is admitted with cough, shortness of breath and 15 lb weight loss. Medical comorbidities include DM and CKD with creatinine clearance 32. ECOG PS: 1. CT chest/abdomen/pelvis reveals left lower lobe mass, mediastinal and contralateral supraclavicular adenopathy, and small left pleural effusion. Additionally PET/CT shows numerous osseous metastases. Brain MRI is negative for brain metastatic disease. What would you do?

A) Perform thoracentesis and send cytology for diagnosis.

B) Perform biopsy of the supraclavicular adenopathy for diagnosis.

C) Perform bone biopsy for diagnosis.

D) Perform bronchoscopy/EBUS with transbronchial biopsy of the left lung mass and mediastinal staging.

Case Study 2

- Patient underwent biopsy of the supraclavicular lymphadenopathy. Pathology showed poorly differentiated adenocarcinoma.
- Biomarker testing included:

- ctDNA identified KRAS G12V, STK11, TP53, and KIT amplification

- PD-L1 was <1%

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Case Study 2

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

  A) Wait for tumor tissue NGS.

  B) Start carboplatin/pemetrexed/pembrolizumab.

  C) Start nivolumab/ipilumumab.

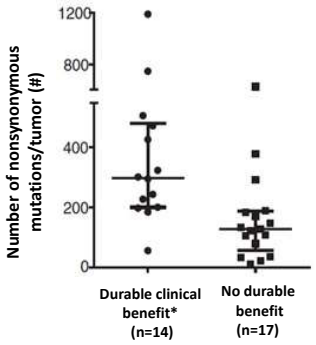
  D) Start nivolumab/ipilumumab/carboplatin/pemetrexed

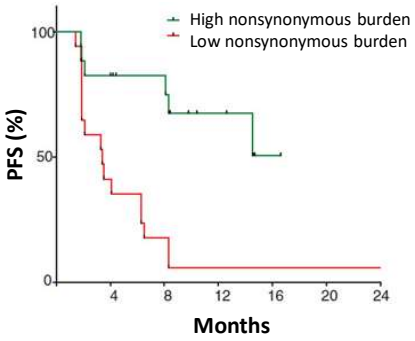
  E) Would holf off on immunotherapy given this patient has an STK11 alteration

Thank you! Questions?

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