sitc Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy for the Treatment of Lung Cancer

Victoria M Villaflor, MD

Associate Professor, Medicine

Robert H. Lurie Cancer Center, Northwestern University

Chicago, Illinois

AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

sitc Society for Immunotherapy of Cancer

Disclosures

- No financial relationships to disclose

- I will not 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

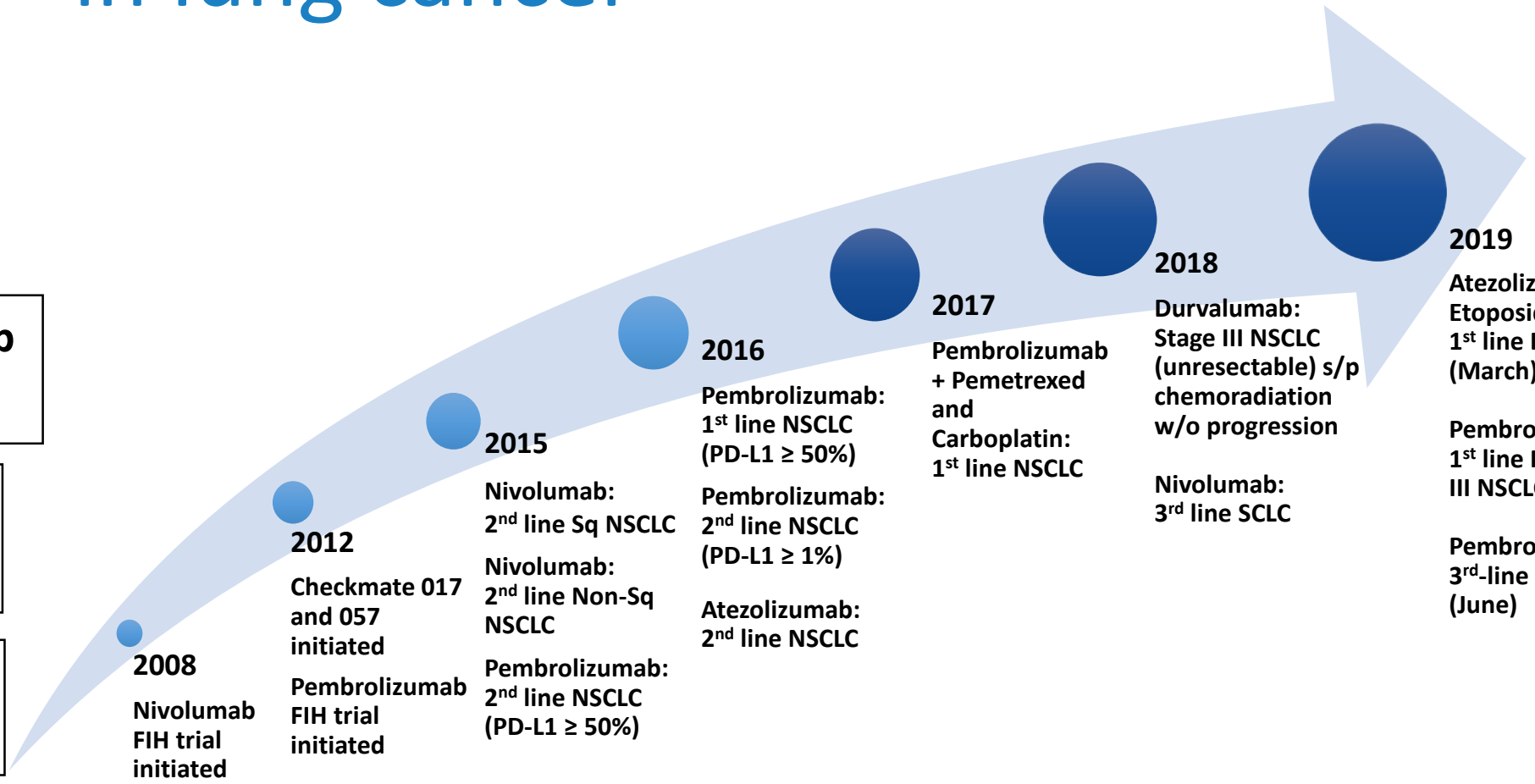
FDA-approved checkpoint inhibitors in lung cancer

Nivolumab
PD-1

Pembrolizumab
PD-1

Atezolizumab
PD-L1

Durvalumab
PD-L1



2008
Nivolumab FIH trial initiated

2012
Checkmate 017 and 057 initiated

Pembrolizumab FIH trial initiated

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 (March)

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

Pembrolizumab: 3rd-line ED-SCLC (June)

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
- **IMPOWER 150** – 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

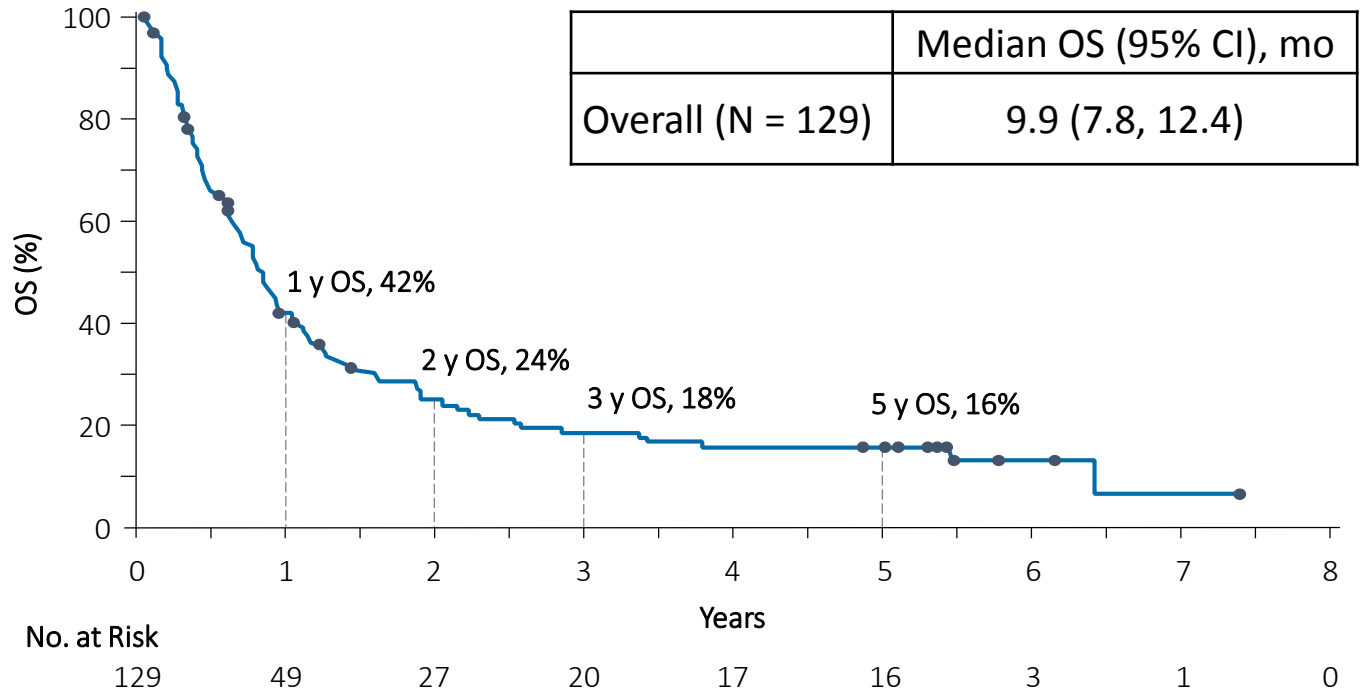
CA209-003: Nivolumab in Heavily-pretreated Advanced NSCLC (NCT00730639)

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)



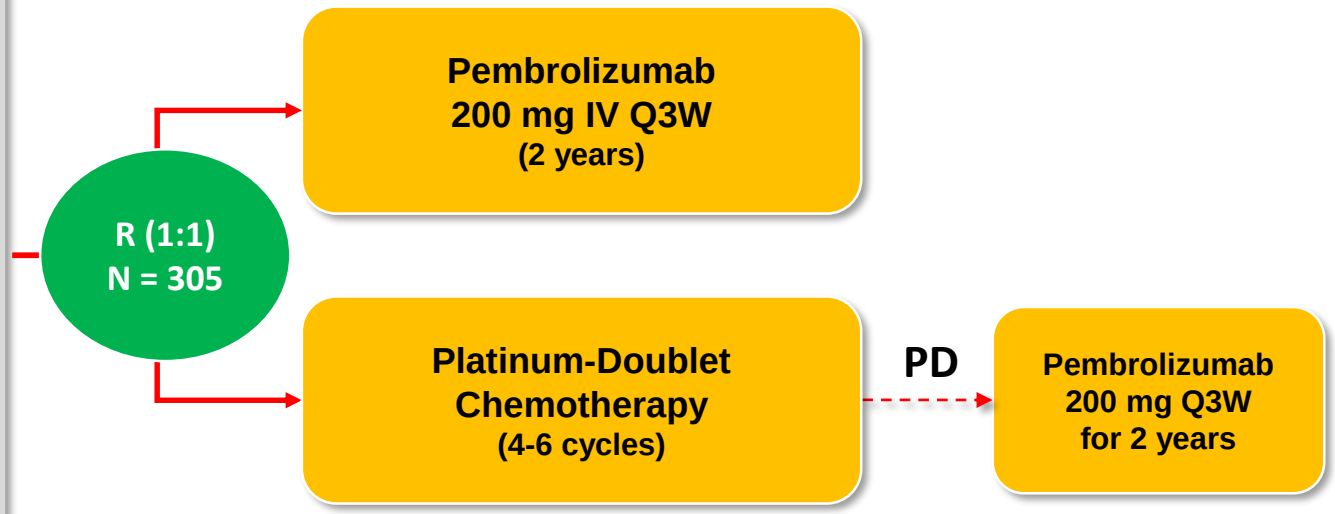
Gettinger et al. JCO 2018
Brahmer et al, AACR 2017
NCI SEER data, Lung and Bronchus Cancer, 2014

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

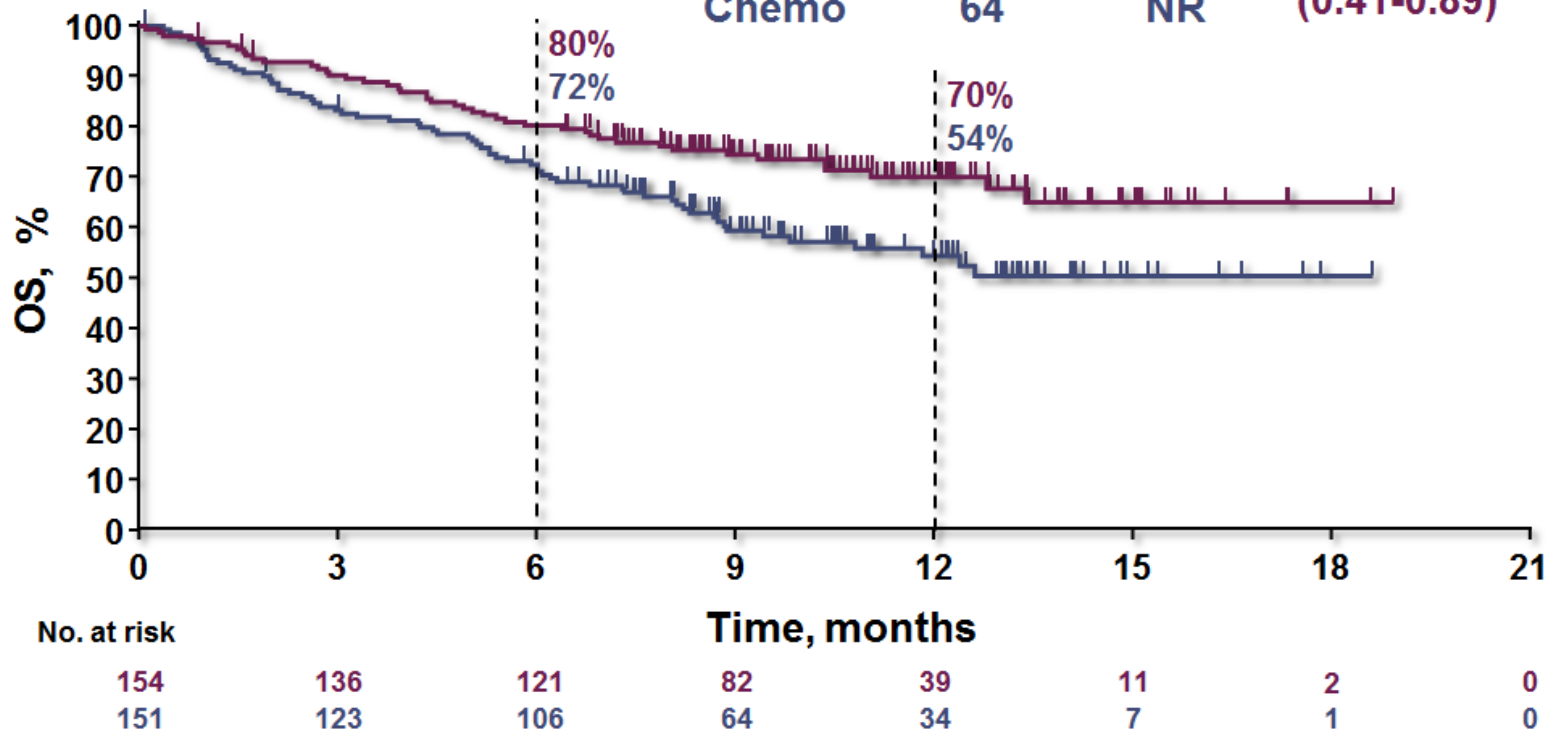


Reck M et al, ESMO 2016, NEJM 2016

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

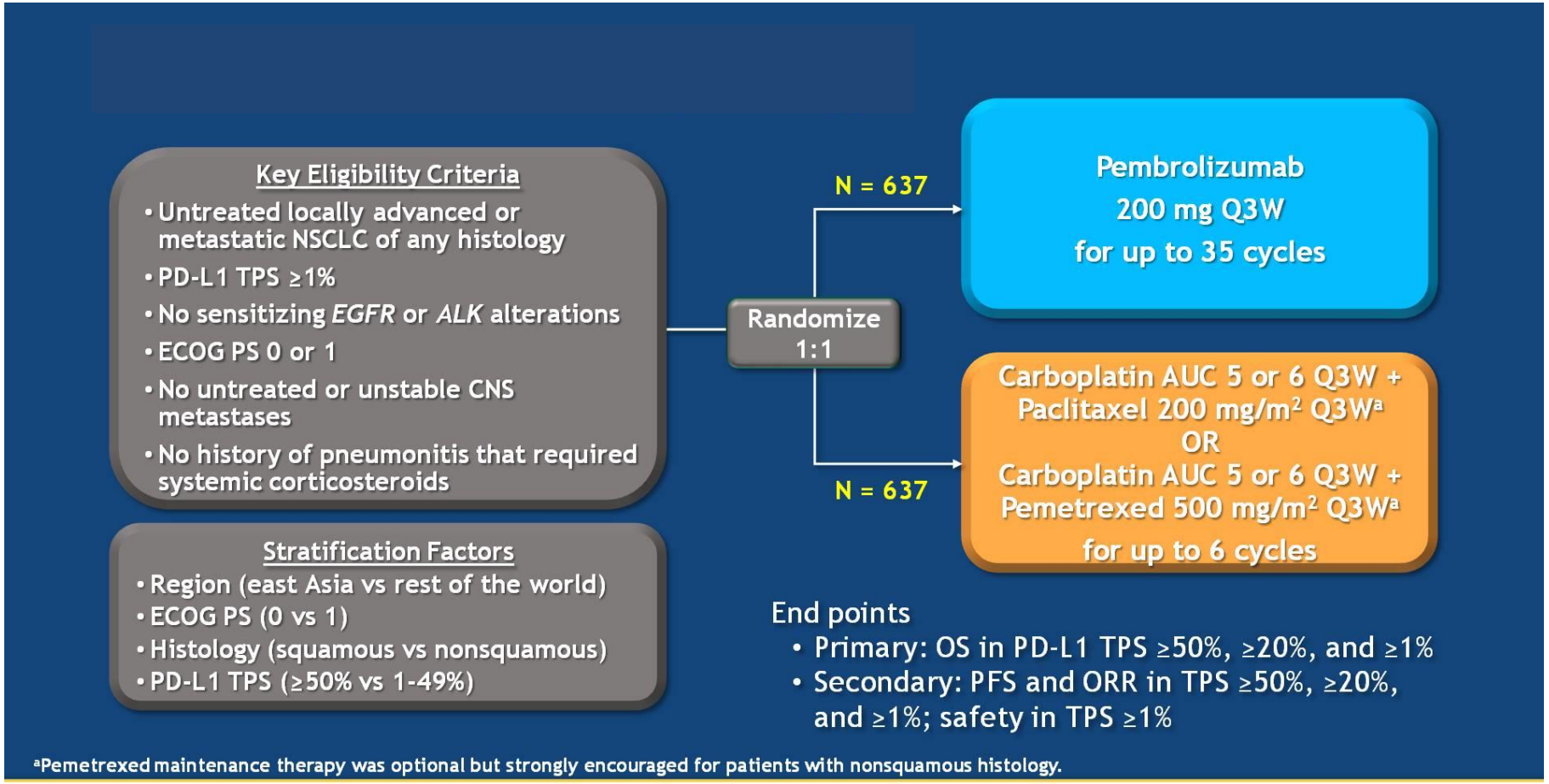
Overall Survival

	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

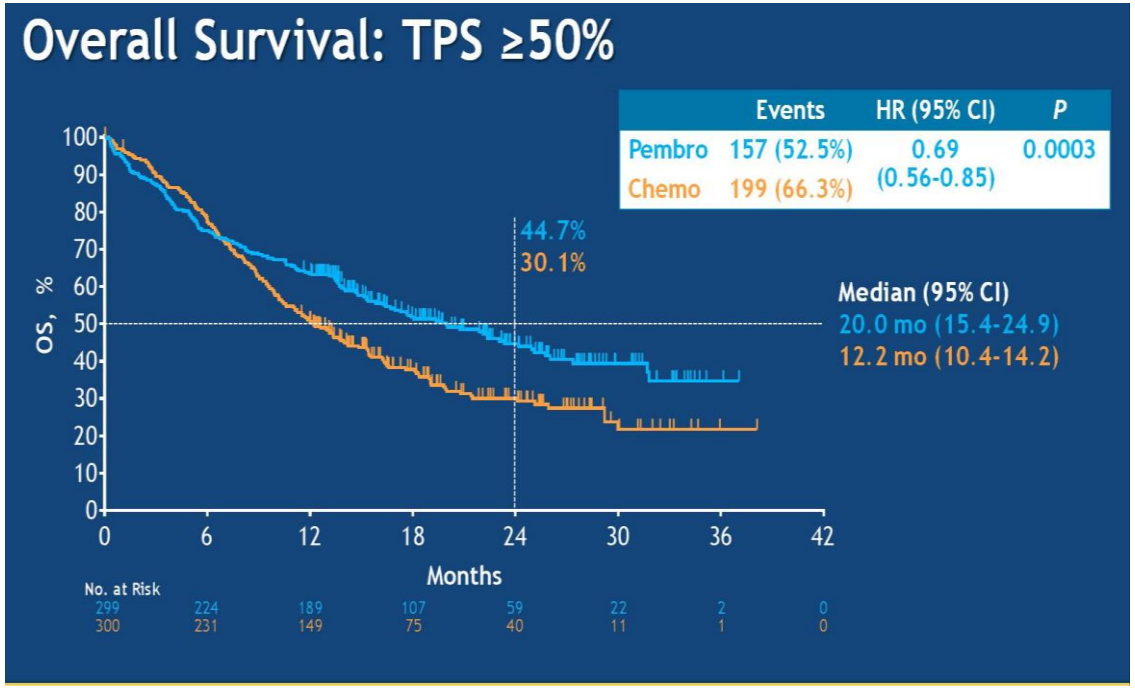
KEYNOTE-042: Pembrolizumab vs. Chemotherapy for PD-L1 ≥ 1% NSCLC

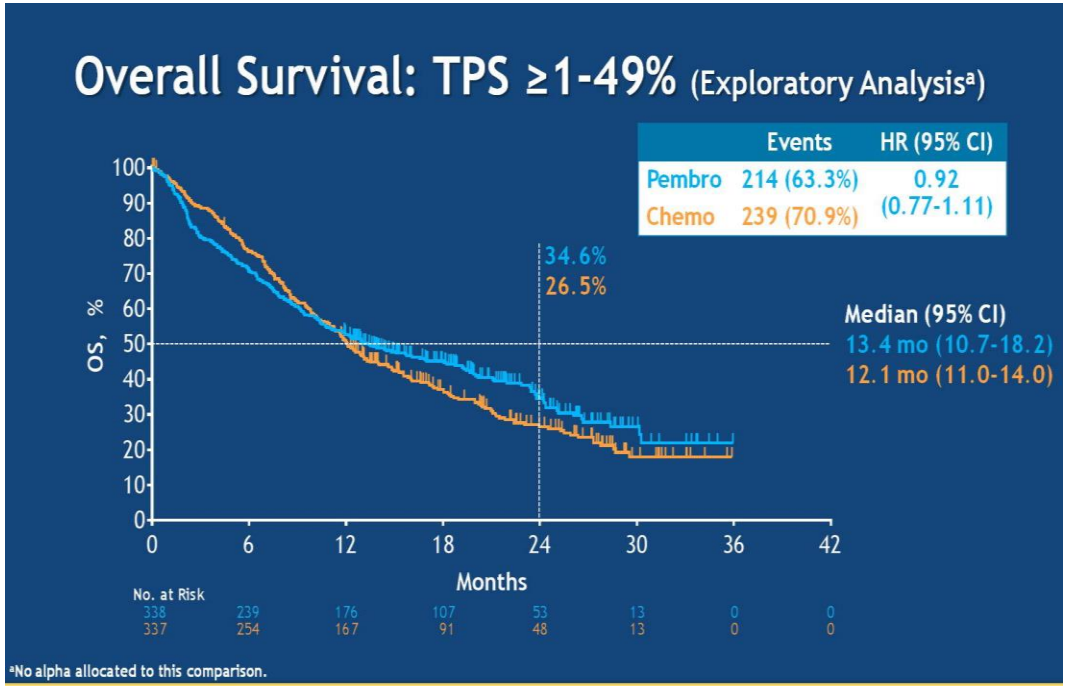


Lopes et al, ASCO 2018

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

Overall Survival

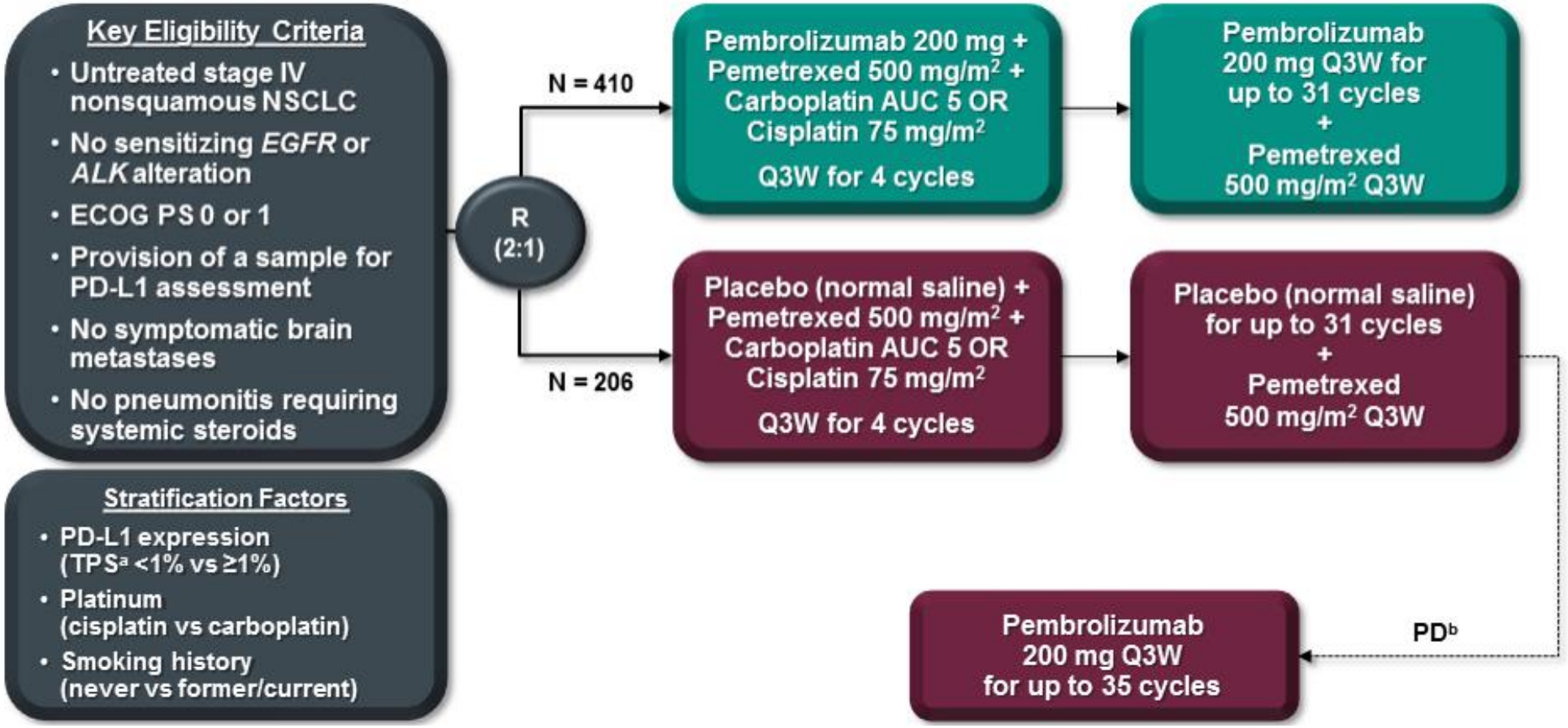




Survival benefit seemed to be driven by the TPS ≥ 50% subset with little benefit witnessed in the subset TPS = 1 - 49%

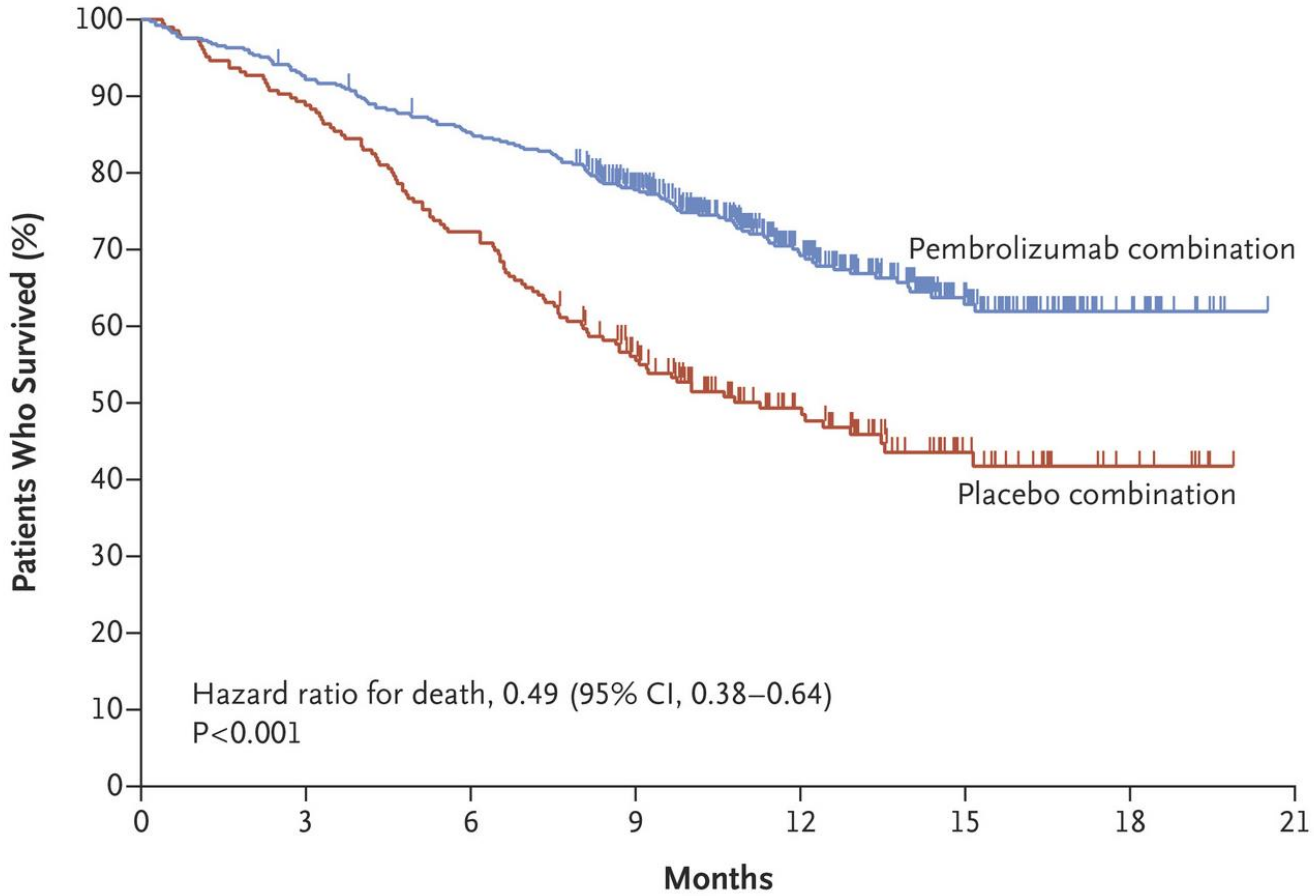
Lopes et al, ASCO 2018

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



Ghandi et al, NEJM 2018

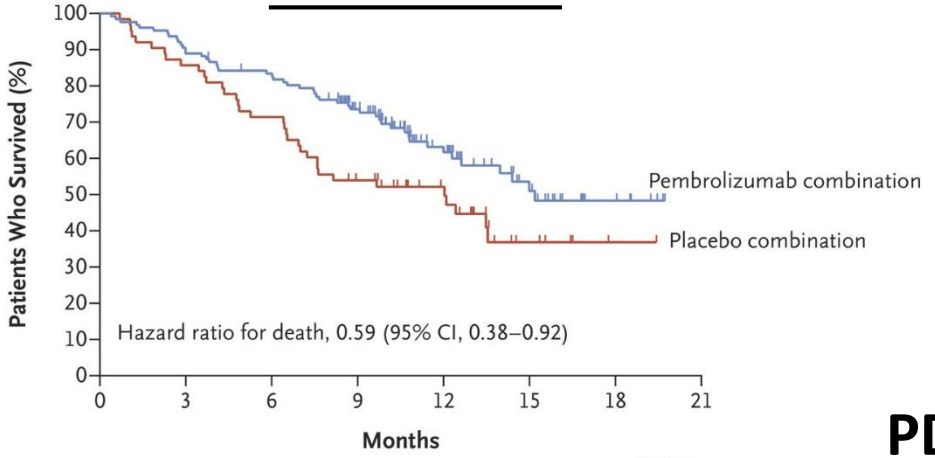
KEYNOTE-189: Pembrolizumab/Platinum /Pemetrexed vs Chemotherapy Alone for Advanced Non-Squamous NSCLC



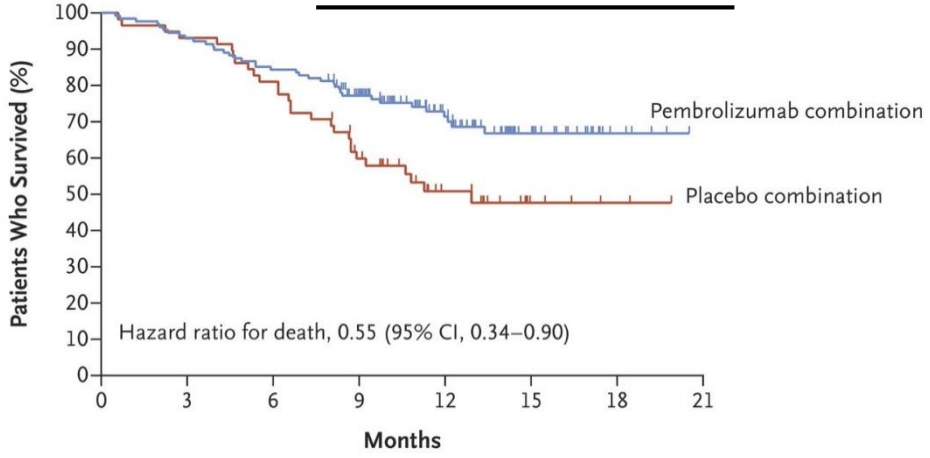
Ghandi et al, NEJM 2018

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

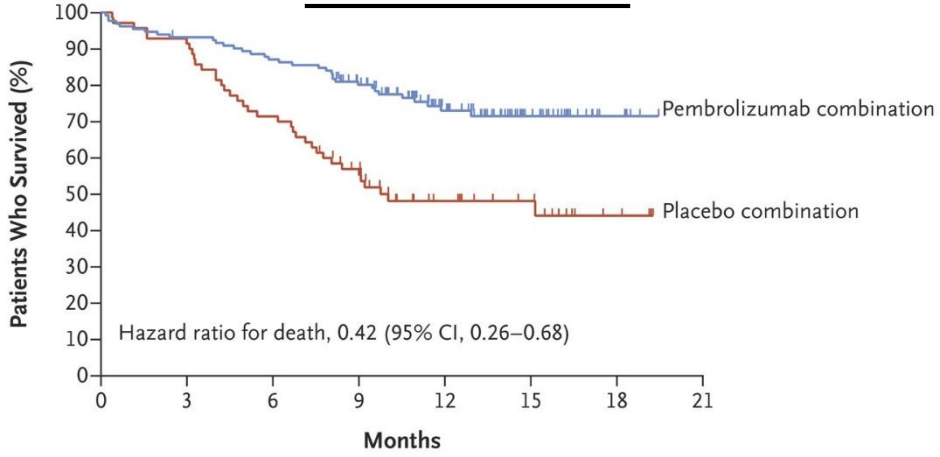
PD-L1 < 1%



PD-L1 = 1 – 49%

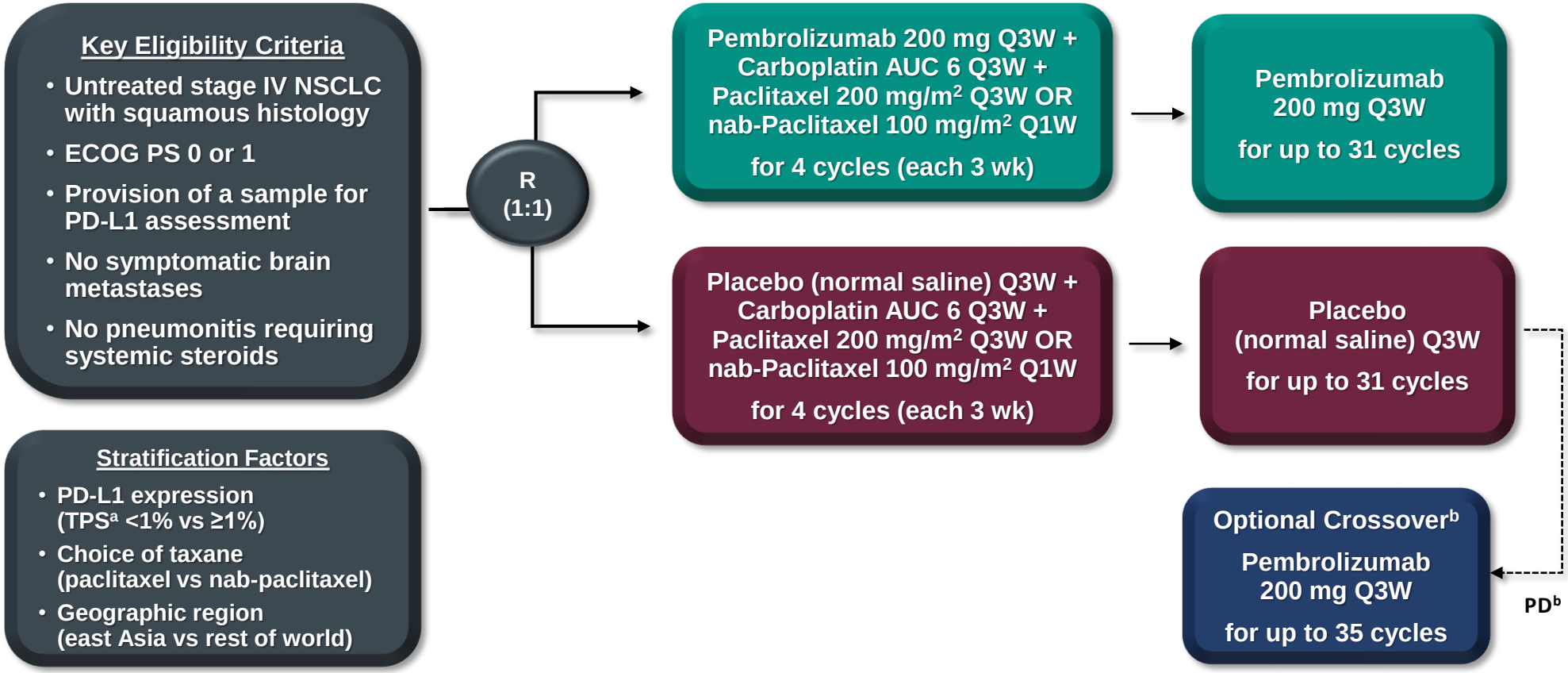


PD-L1 ≥ 50%



Ghandi et al, NEJM 2018

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

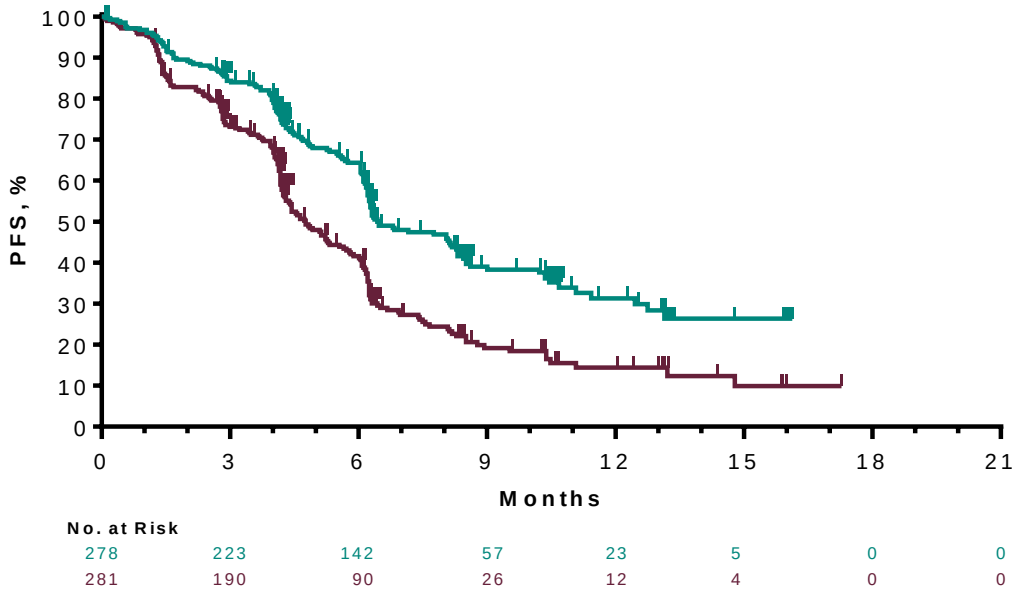


Paz-Ares et al, ASCO 2018

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

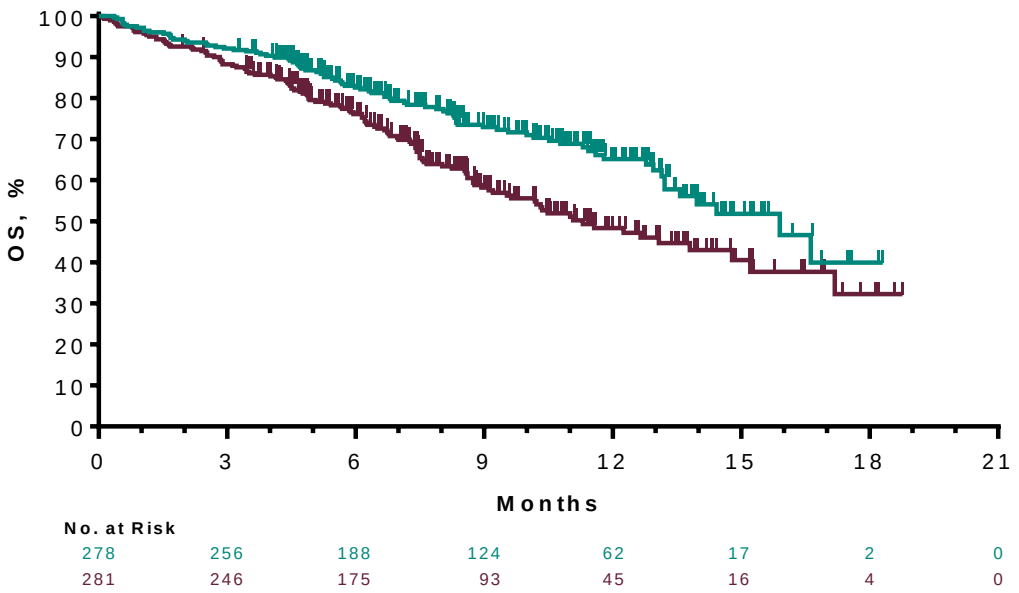
PFS (RECISTv1.1, BICR)

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



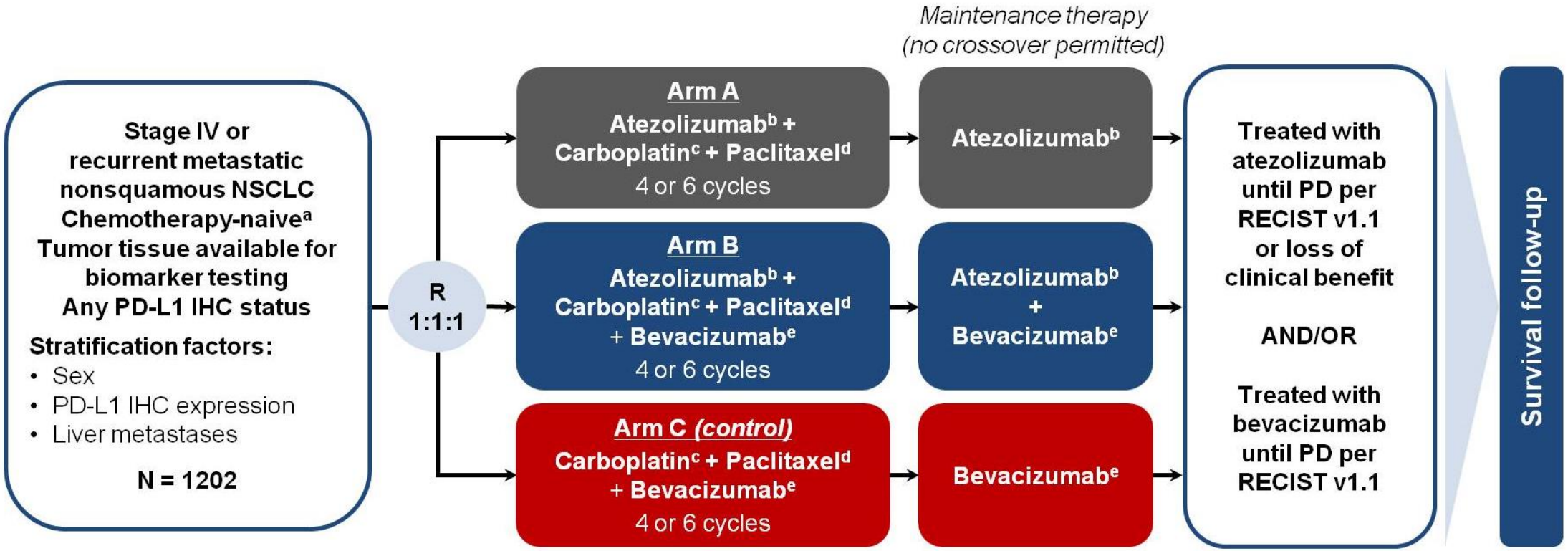
Overall Survival

	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

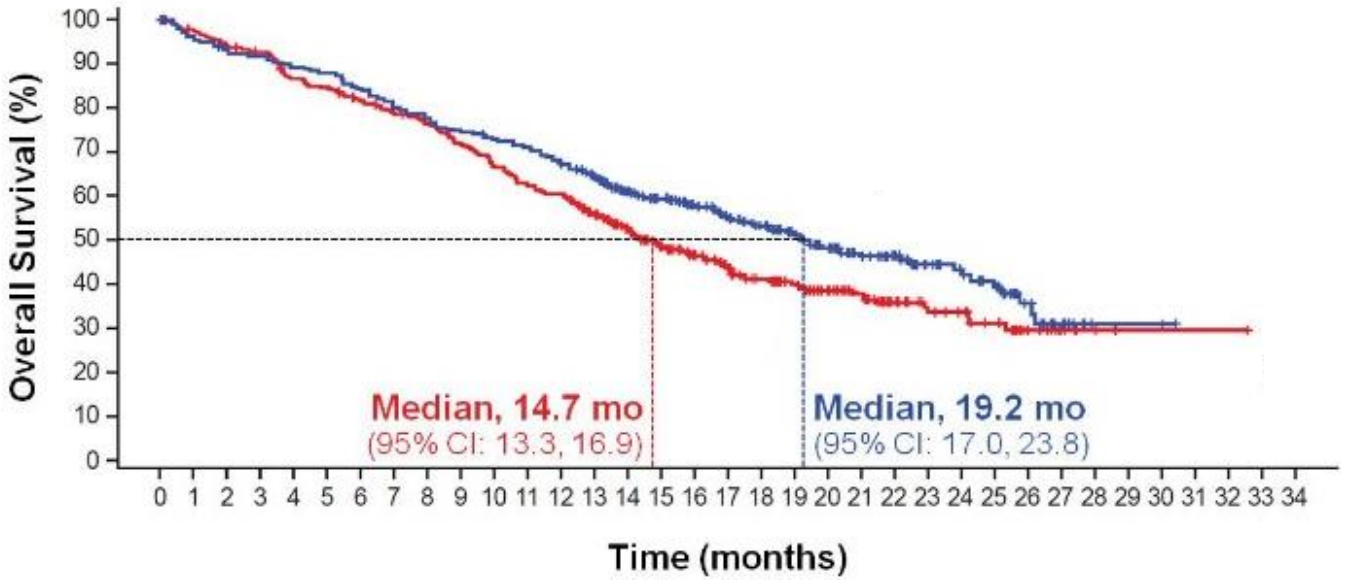


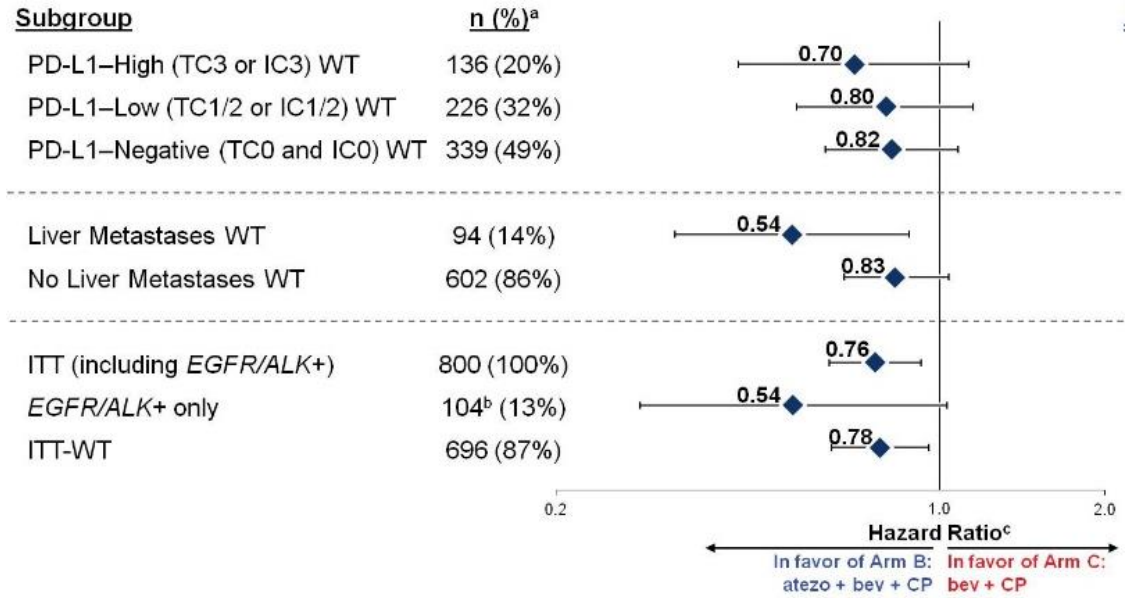
Socinski et al, NEJM 2018

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

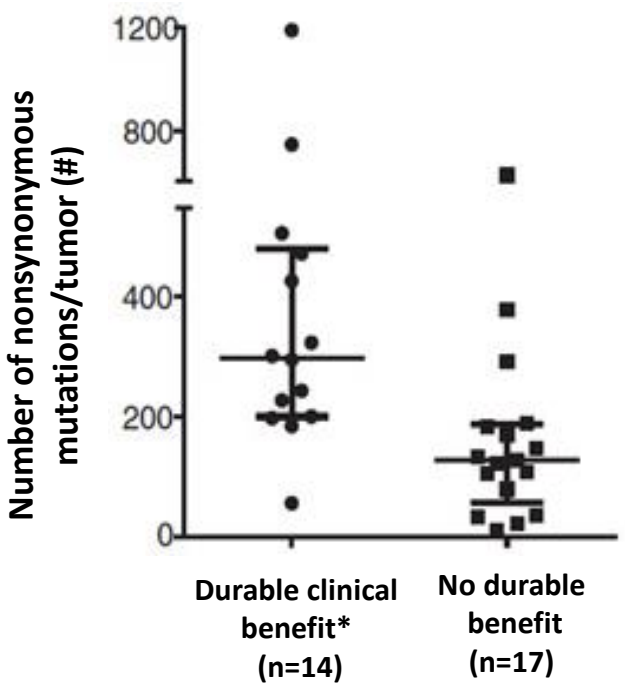


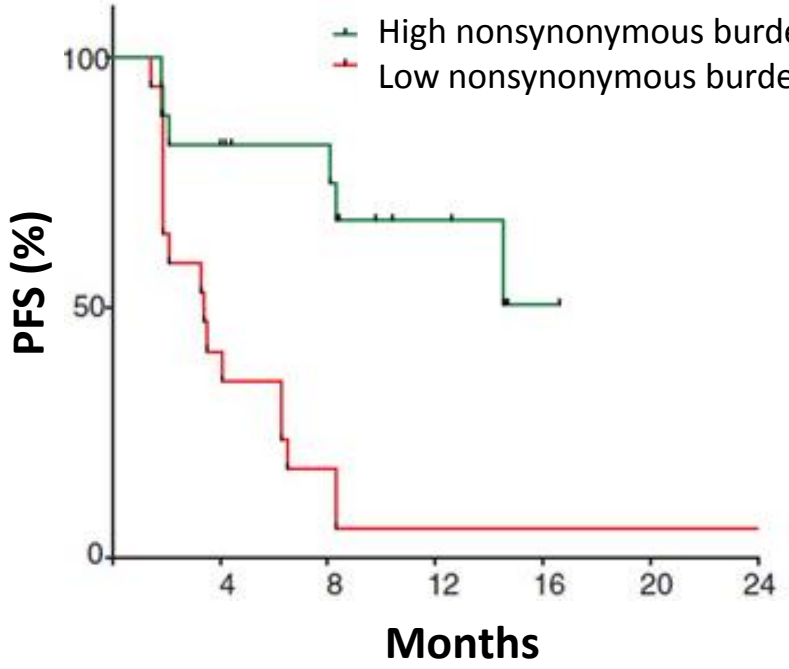


Socinski et al, NEJM 2018

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.

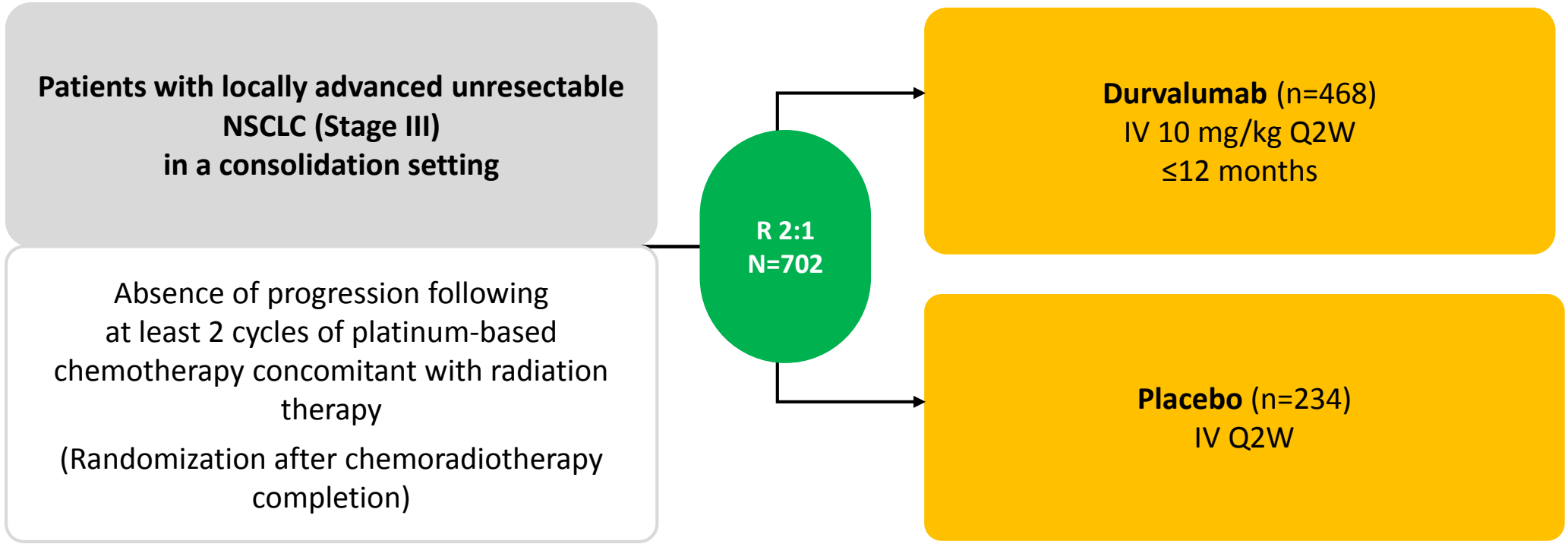




*Partial or stable response lasting > 6 mo

Rizvi N et al, Science, 2015

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

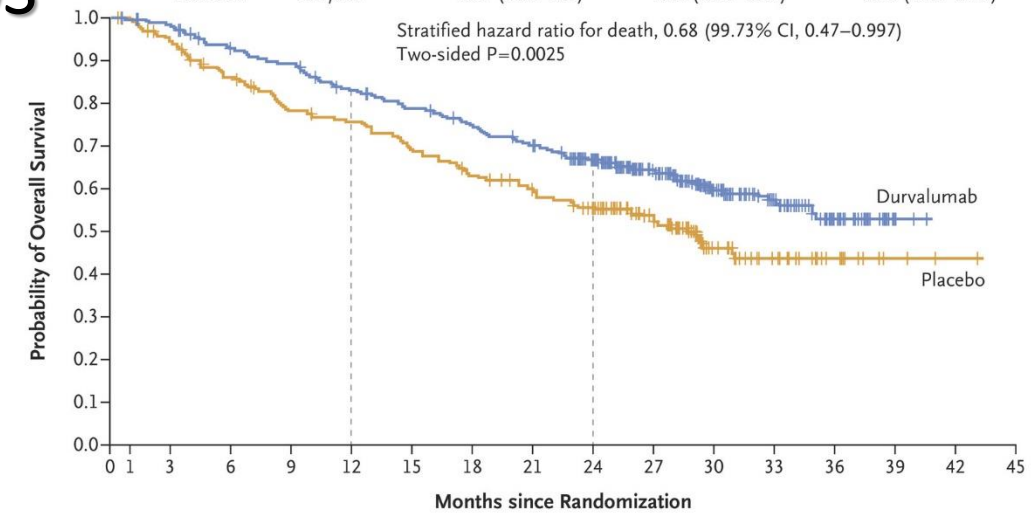


In House Data, AstraZeneca Pharmaceuticals LP. PACIFIC Protocol. 2014.
NIH 2015 NCT02125461, http://clinicaltrials.gov/ct2/show/NCT02125461.
Creelan B, Iannotti NO, Salamat MA, et al. 2016. (PHRR150325-000989)
Ann Oncol. 2015;26 (supplement 1): i24-i28, abstract 95TiP.

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

OS

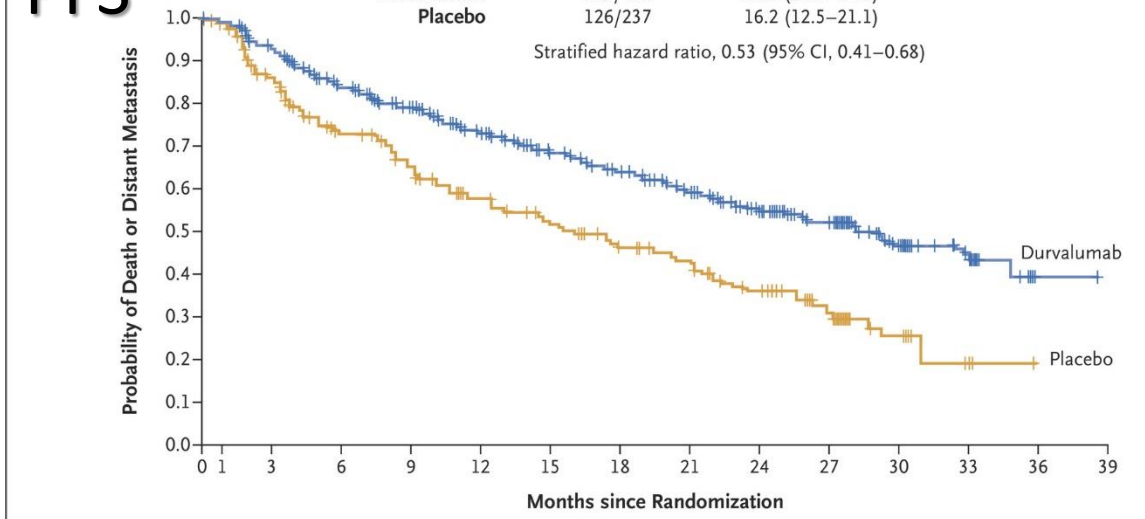
	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



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)

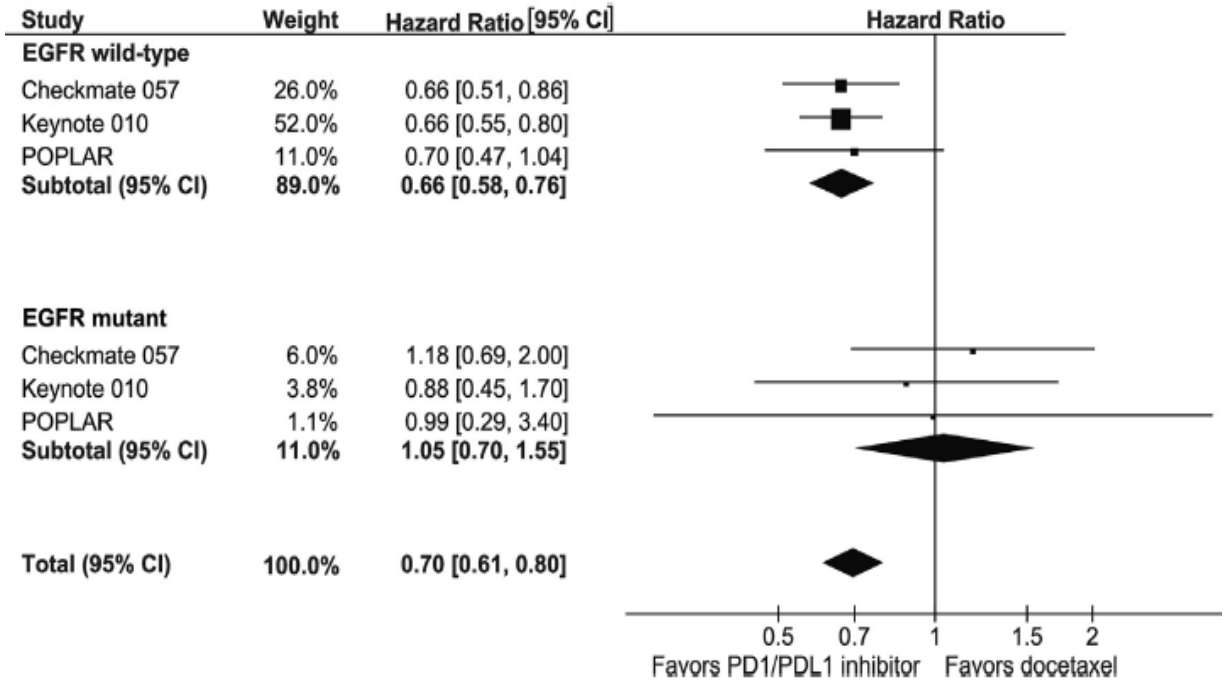


No. at Risk														
Durvalumab	476	419	357	316	259	223	194	163	129	92	46	25	1	0
Placebo	237	189	139	118	95	77	64	54	39	27	12	5	0	0

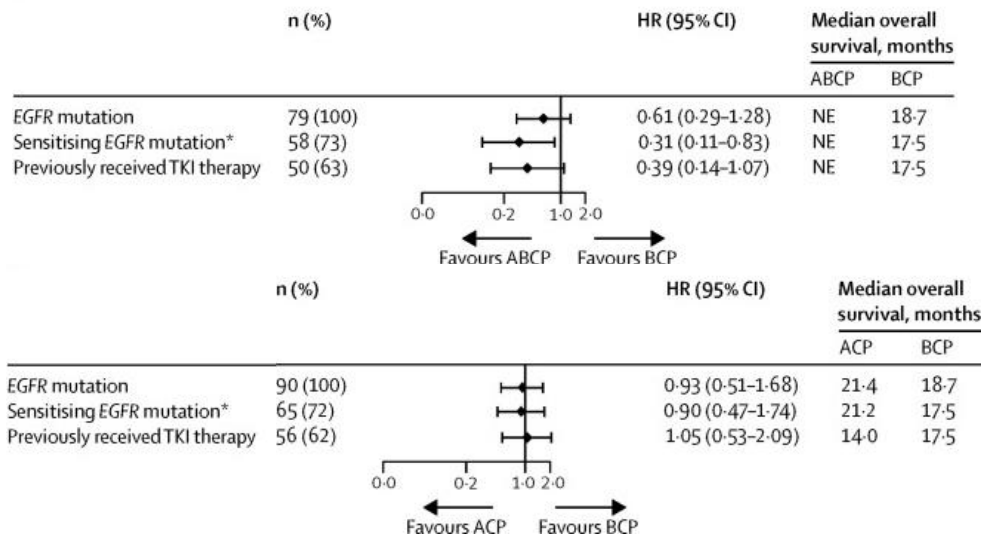
Antonia et al, NEJM 2018

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

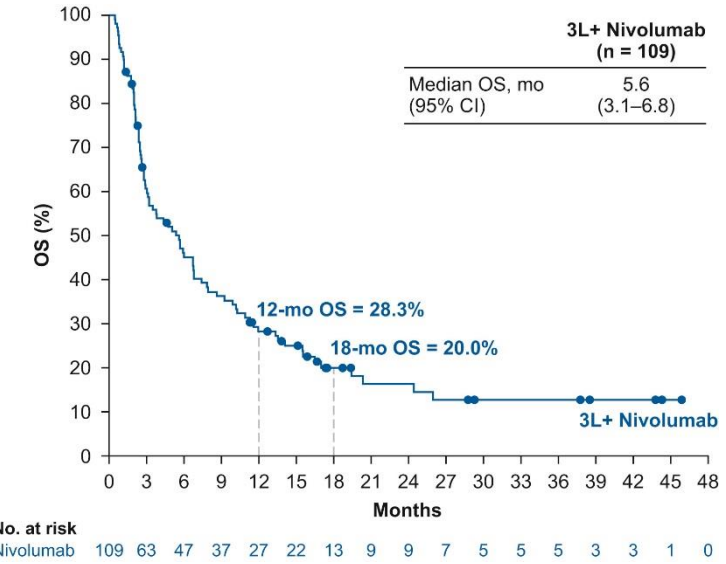
- 10-15% of lung cancers
- Almost exclusively former/current smokers
- Median survival 1-2 years after diagnosis
- Until recently, only one FDA-approved 2nd line option: topotecan – DOR: 3.3 months
- Recent approvals of immunotherapies mark the first progress in decades

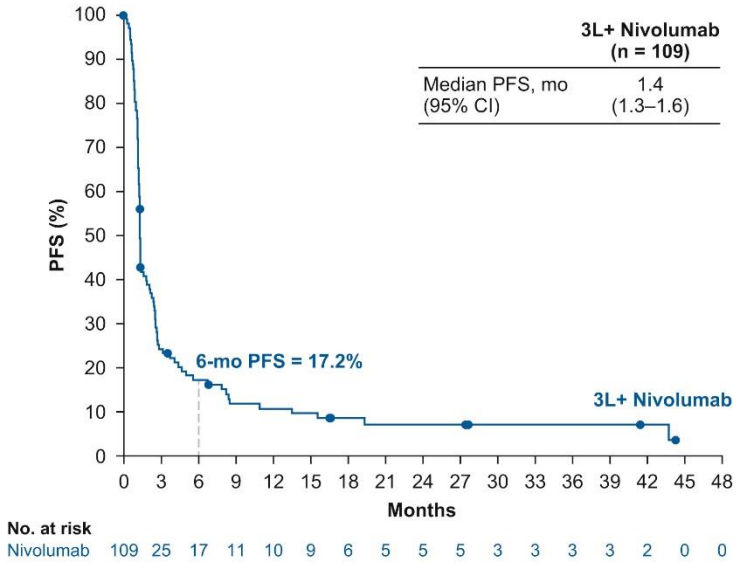
Approved checkpoint inhibitors in SCLC

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

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



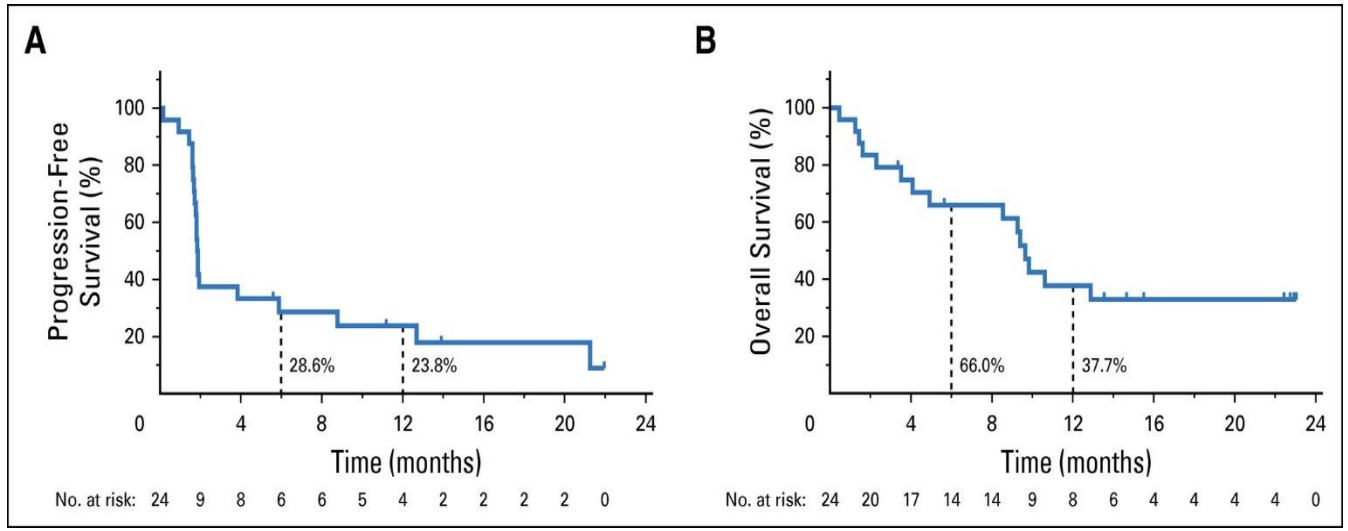


Ready, J Thorac Oncol 2019

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

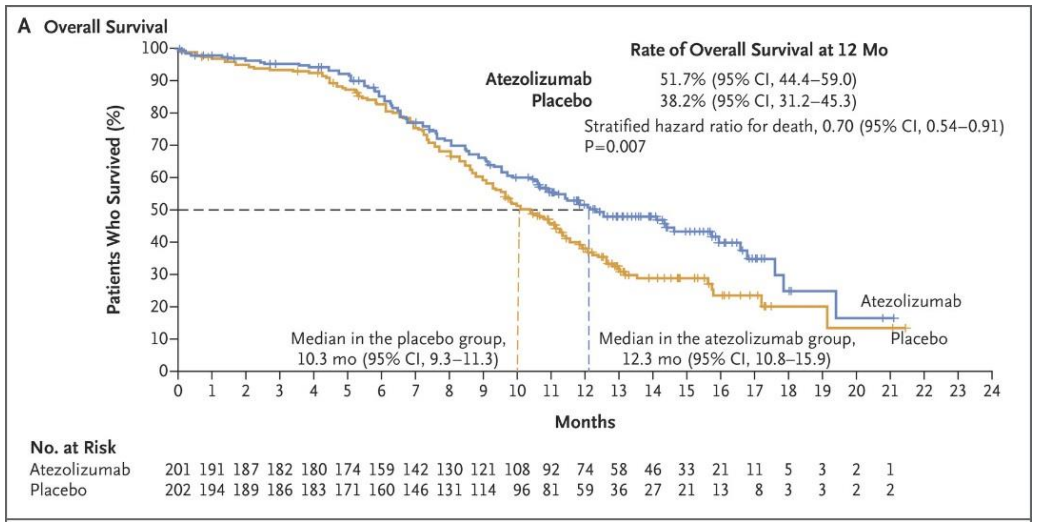
PD-L1+ (KEYNOTE-028)



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

- NSCLC has been a proving ground for checkpoint inhibitors
- Moving from 2nd/3rd line options to the front line
- Clear-cut biomarkers still lacking

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

- 73 yo AA male, history of larynx SCC 6 yrs prior → TPF X 2, Radiation to larynx, f/b adjuvant everolimus on clinical trial
  - PMHx: **CAD, COPD-requires oxygen,** HTN, H/O laryngeal cancer, BPH
  - Soc Hx: 16 pk-yr cigarettes, f/b cigars X 20 yrs, Hx of heavy ETOH use - quit both 12 yrs ago.
- Presents to ED with SOB, cough, white sputum, wt loss, tachycardia and LE edema
- PE: Thin, frail appearing, 2L 02NC, ECOG PS =1, CVS Irregular/tachycardic, diminished Breath sounds thruout and 2+ edema BLE
- Labs: Unremarkable for CBC, Crea -1.5, Albumin 3.0 otw, CMP wnl.

Case Study 1

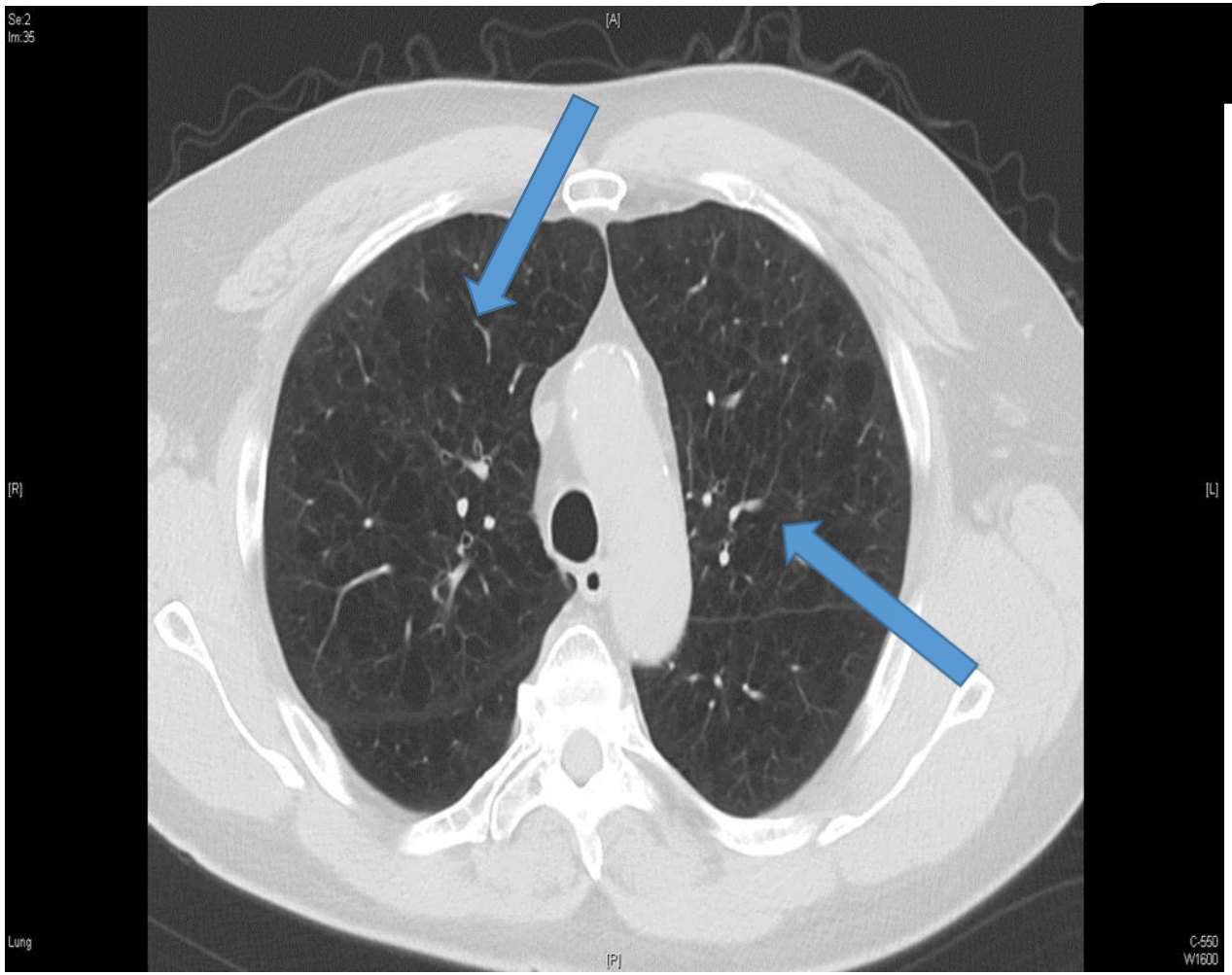
- What would you do next?
  a) EKG and CT angiogram/PE protocol f/b ECHO and troponin
  b) Diuretics
  c) Steroids, albuterol/atrovent nebulizer treatment
  d) Antibiotics

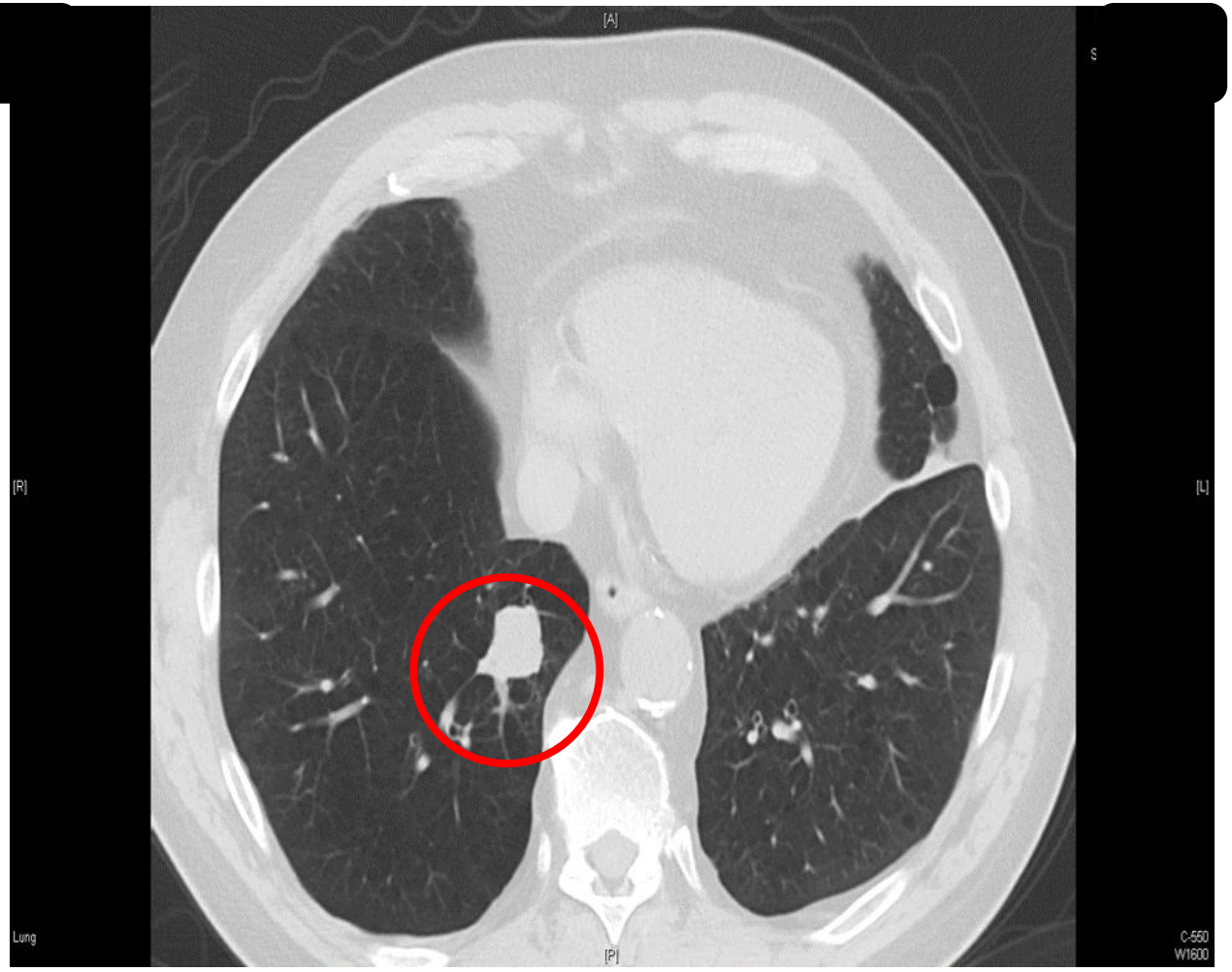
Case Study 1

- What would you do next?
  - **a) EKG and CT angiogram/PE protocol f/b ECHO and troponin**
    - This option is reasonable, if someone has a history of cancer, tobacco history and swollen ankles one's differential diagnosis should be: PE, AMI, CHF, Pneumonia vs COPD exacerbation. Any of these can be ruled in with this workup.
  - b) Diuretics
    - This option is the least reasonable, this assumes fluid overload without accounting for all symptoms.
  - c) Steroids, albuterol/atrovent nebulizer treatment
    - This is a reasonable option, testing first needs to be done to ensure not a PE or cardiac as steroids and nebulizer treatments will be helpful for COPD exac only.
  - d) Antibiotics
    - This is a reasonable option, testing first needs to be done to ensure not a PE or cardiac. Additionally, in a frail patient, WBC and temperature may not be elevated and CT will tell us if there is an obstructive process as antibiotic choice may differ.

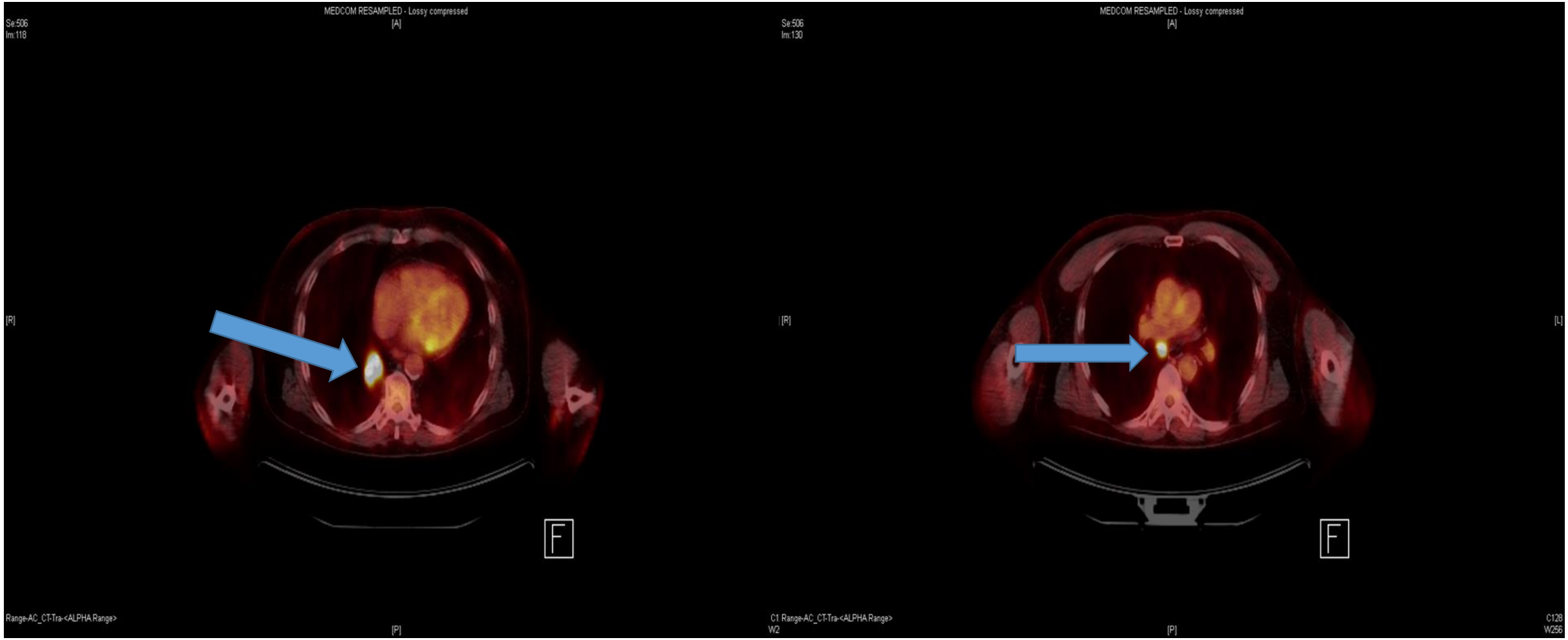
Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Case Study 1





Case Study 1



Case Study 1

- EBUS biopsy done, c/w Adenocarcinoma CD7/TTF1 +, PDL1 5%, EGFR/ALK/ROS1/BRAF/KRAS negative. What is your next recommendation?
  a) Thoracic surgery consultation for Right lower lobectomy
  b) Radiation consultation for CRT
  c) Radiation consultation for CRT f/b checkpoint inhibitor
  d) Chemotherapy with concurrent checkpoint inhibition
  e) Checkpoint inhibitor single agent

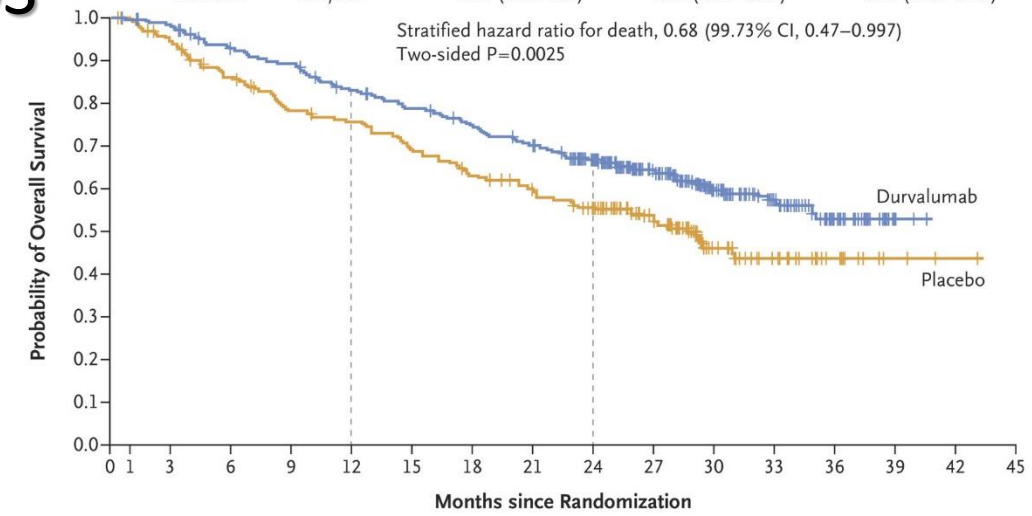
Case Study 1

- EBUS biopsy done, c/w Adenocarcinoma CD7/TTF1 +, PDL1 5%, EGFR/ALK/ROS1/BRAF/KRAS negative. What is your next recommendation?
  - a) Thoracic surgery consultation for Right lower lobectomy
    - This pt has L7 (N2) disease, requires oxygen, CAD etc. Not a good surgical candidate, and N2 disease – clearly Stage III
  - b) Radiation consultation for CRT
    - Very reasonable option
  - **c) Radiation consultation for CRT f/b checkpoint inhibitor**
    - Most reasonable option based on PACIFIC trial for a inoperable patient to be treated with curative intent
  - d) Chemotherapy with concurrent checkpoint inhibition
    - This would be reasonable, if not potentially curable (stage III)
  - e) Checkpoint inhibitor
    - Single agent checkpoint inhibitor would be appropriate if not curative intent and PDL1 $\geq$ 50%

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

OS

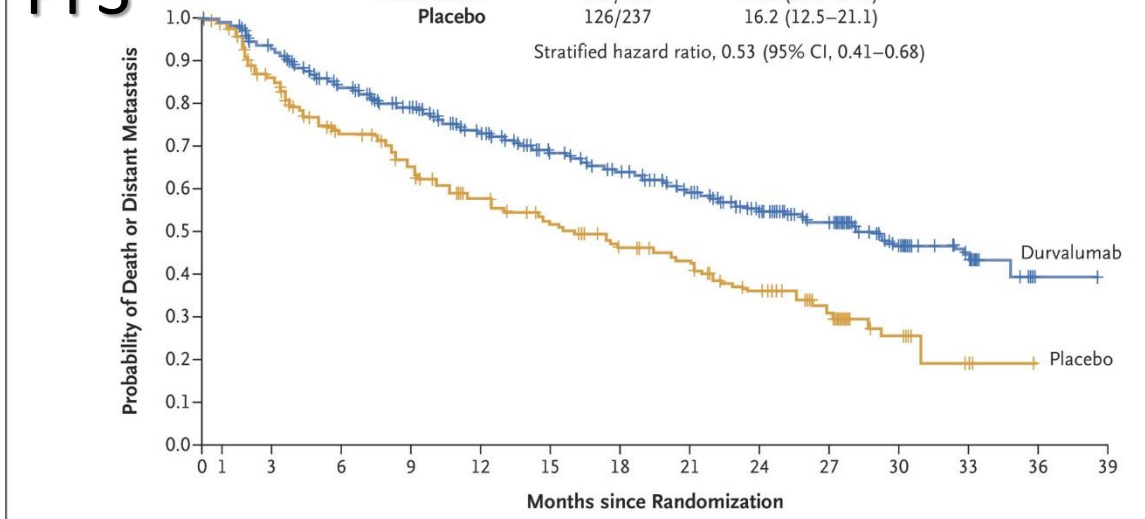
	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



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

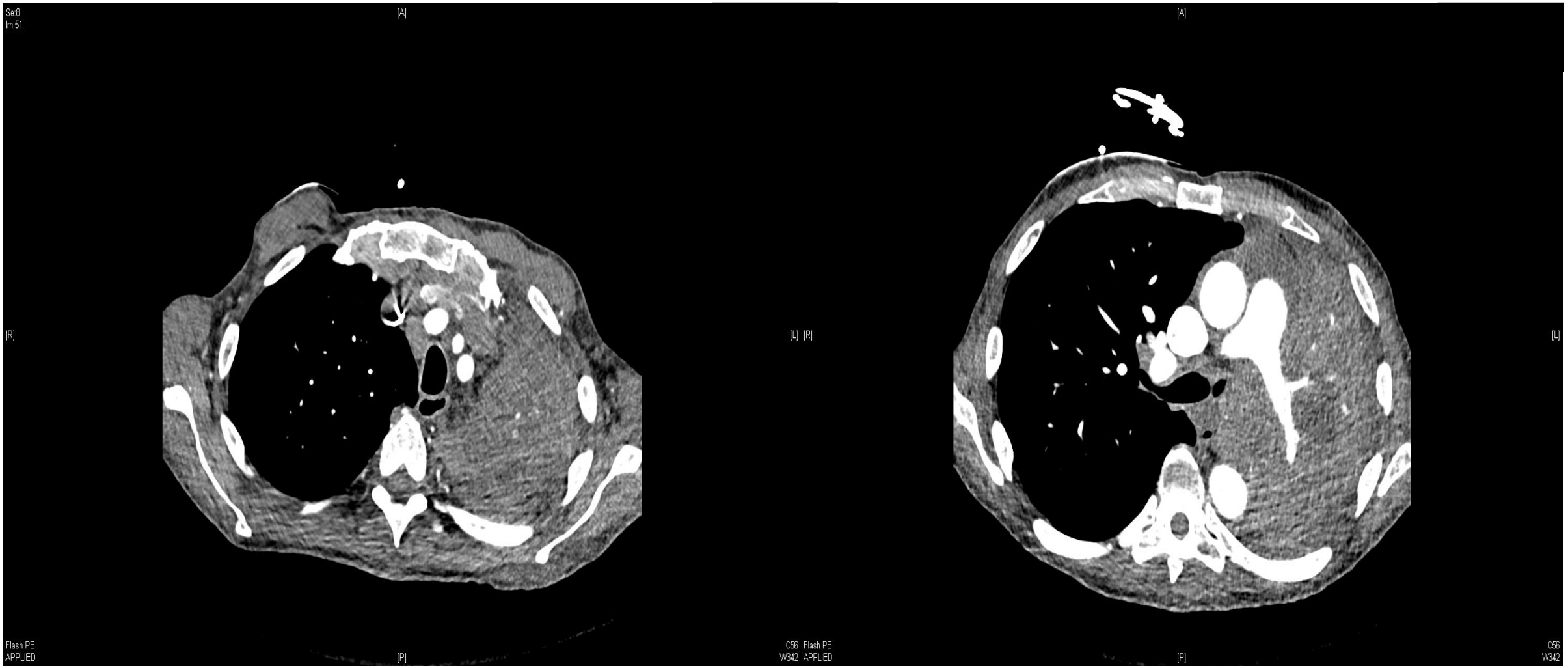
Case Study 1

- This patient with cT2N2M0 AC, PDL1 5% underwent CRT with curative intent.
  - Chemo used with XRT - Carbo/Taxol, no consolidation chemotherapy
  - Started on Durvalumab as consolidative therapy per the PACIFIC trial
  - Is now 1 year out, doing well with NED

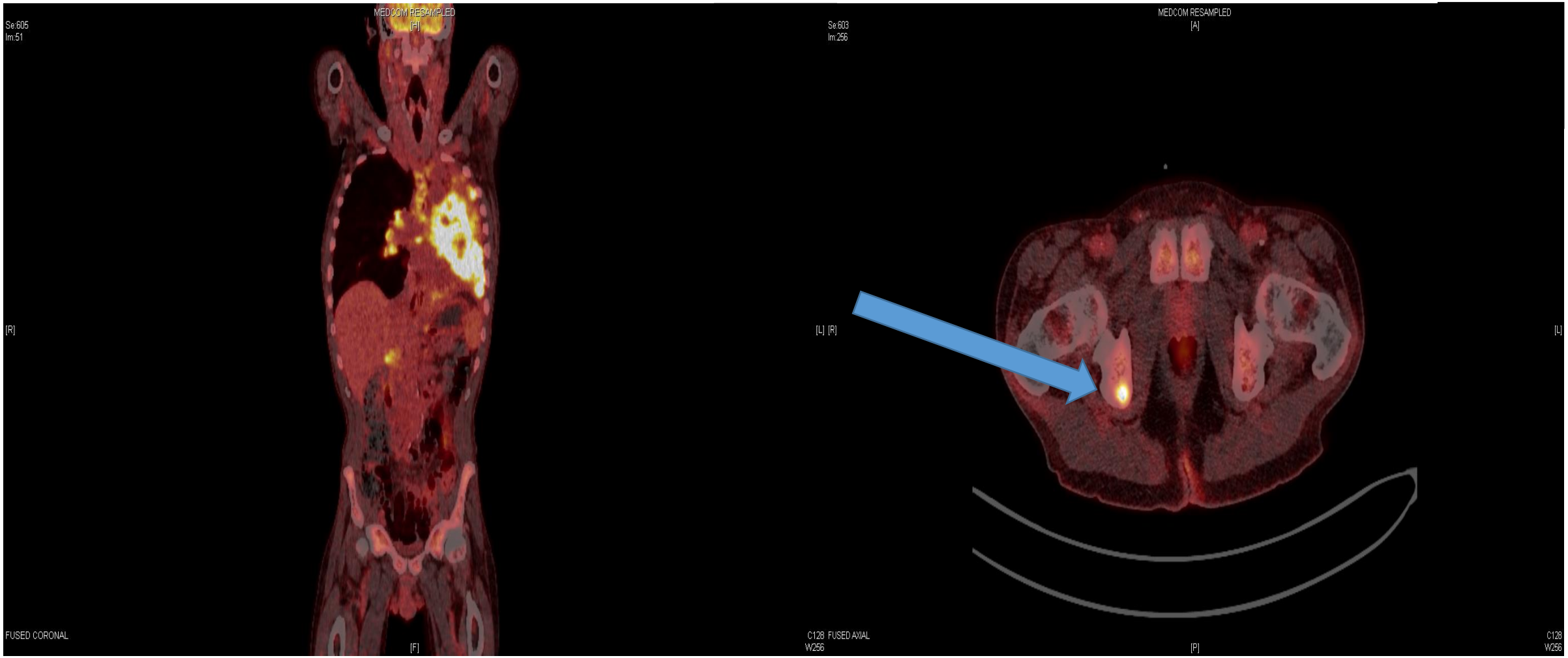
Case Study 2

- Patient is a 62 yo male who presented with 1 year increasing weight loss **(50#),** cough and SOB admitted to hospital for SOB and weakness.
  - PMHx: **A-fib, COPD – 4L oxygen,** HTN, Hyperthyroid controlled on tapazole
  - Soc Hx: Tobacco 80 pk-yrs, still smoking.
- PE: Thin, frail appearing in wheelchair **on 4L Oxygen NC**, ECOG PS 1, CVS Irregular/tachycardic, diminished Breath sounds thruout **L lung**
- Labs: Unremarkable for CBC, Crea -1.4, Albumin 2.6 otw, CMP wnl.

Case Study 2



Case Study 233



Case Study 2

- CT guided biopsy done, c/w Squamous cell carcinoma, PDL1 10%, EGFR/ALK/ROS1/BRAF/KRAS negative. What is your next recommendation?
  a) Thoracic surgery consultation for L pneumonectomy
  b) Radiation consultation for CRT f/b Checkpoint inhibitor
  c) Chemotherapy with platinum based therapy
  d) Chemotherapy with concurrent checkpoint inhibition
  e) Checkpoint inhibitor as single agent

Case Study 2

- CT guided biopsy done, c/w Squamous cell carcinoma, PDL1 10%, EGFR/ALK/ROS1/BRAF/KRAS negative. What is your next recommendation?

a) Thoracic surgery consultation for L pneumonectomy
   - This patient has cT4N3M1C, not appropriate for surgical resection

b) Radiation consultation for CRT f/b Checkpoint inhibitor
   - This patient has cT4N3M1C, not appropriate for curative intent CRT f/b CPI

c) Chemotherapy with platinum based therapy
   - This is a reasonable option but, based on the KEYNOTE 407 study there is a better option. This would be more appropriate if he had a contraindication to checkpoint inhibition

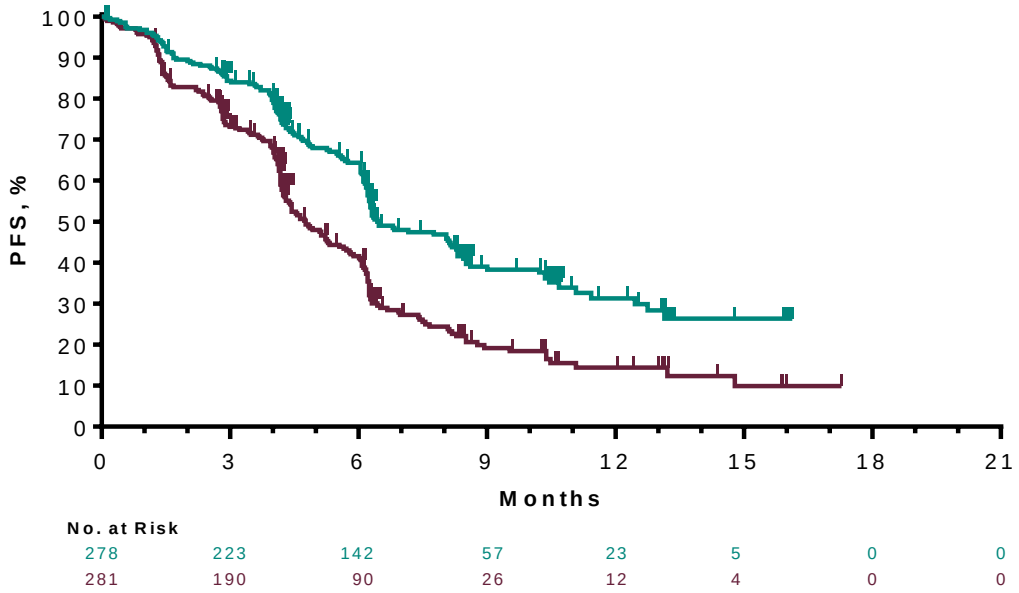
d) **Chemotherapy with concurrent checkpoint inhibition**
   - This is the best option but, based on the KEYNOTE 407 study in a patient with widely metastatic SCC. Would also add denosumab or a bisphosphonate for bone mets, hypercalcemia.

e) Checkpoint inhibitor as single agent
   - Based on KEYNOTE 24 and KEYNOTE 42 – this patient has PDL1 -10% so single agent would not have as good of an outcome as concurrent chemotherapy and CPI

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

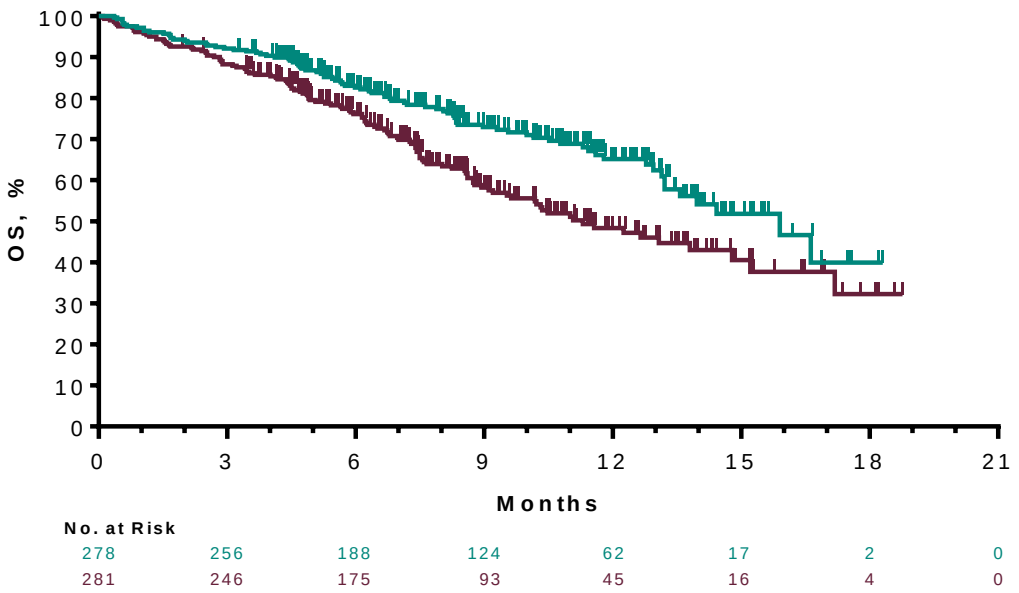
PFS (RECISTv1.1, BICR)

	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

Case Study 2

- What is patient case study #2 instead was a neversmoker, CT guided biopsy done, c/w adenocarcinoma, PDL1 90%, EGFR L858R mutated. What is your next recommendation?
  a) Thoracic surgery consultation for L pneumonectomy
  b) Radiation consultation for CRT f/b Checkpoint inhibitor
  c) Osimertinib as single agent
  d) Chemotherapy with concurrent checkpoint inhibition
  e) Checkpoint inhibitor as a single agent

Case Study 2

- What is patient case study #2 instead was a neversmoker, CT guided biopsy done, c/w adenocarcinoma, PDL1 90%, EGFR L858R mutated. What is your next recommendation?

a) Thoracic surgery consultation for L pneumonectomy
   - This patient has cT4N3M1C, not appropriate for surgical resection

b) Radiation consultation for CRT f/b Checkpoint inhibitor
   - This patient has cT4N3M1C, not appropriate for curative intent CRT f/b CPI

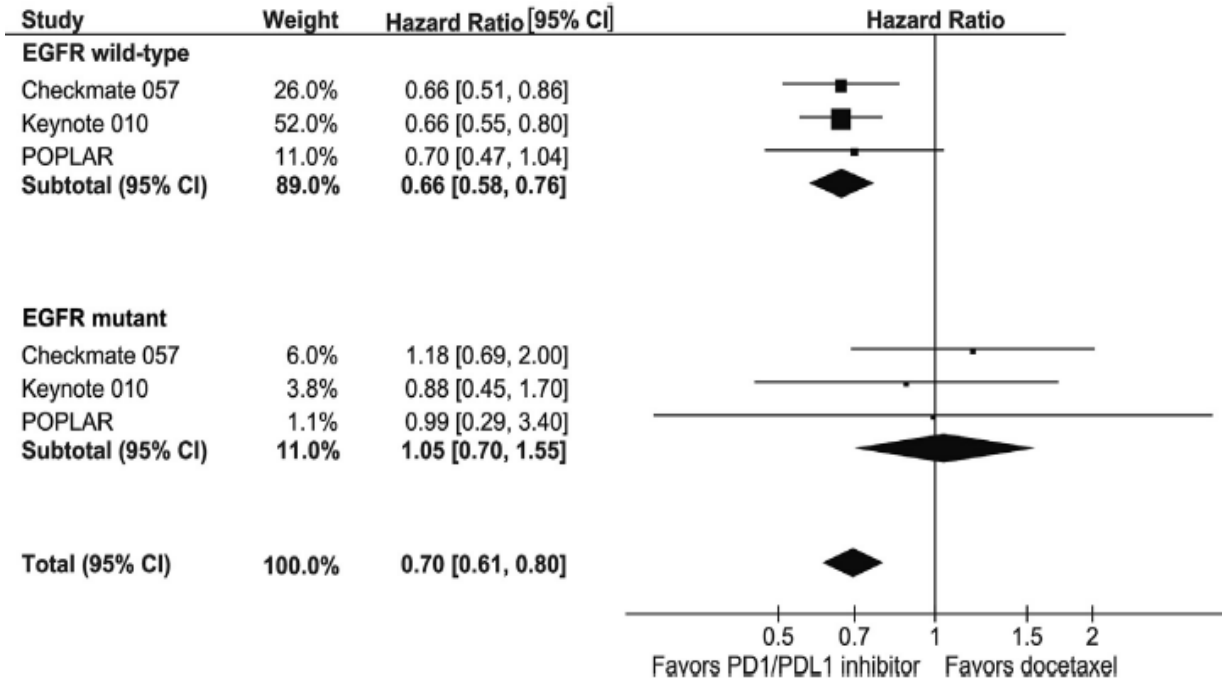
c) Osimertinib as single agent
   - This is the best option based on the Flaura trial and Meta-Analysis of CheckMate 057, KEYNOTE 010, Poplar, and IMPOWER 150 data

d) Chemotherapy with concurrent checkpoint inhibition
   - Driver mutation – better response with EGFR inhibitor as above

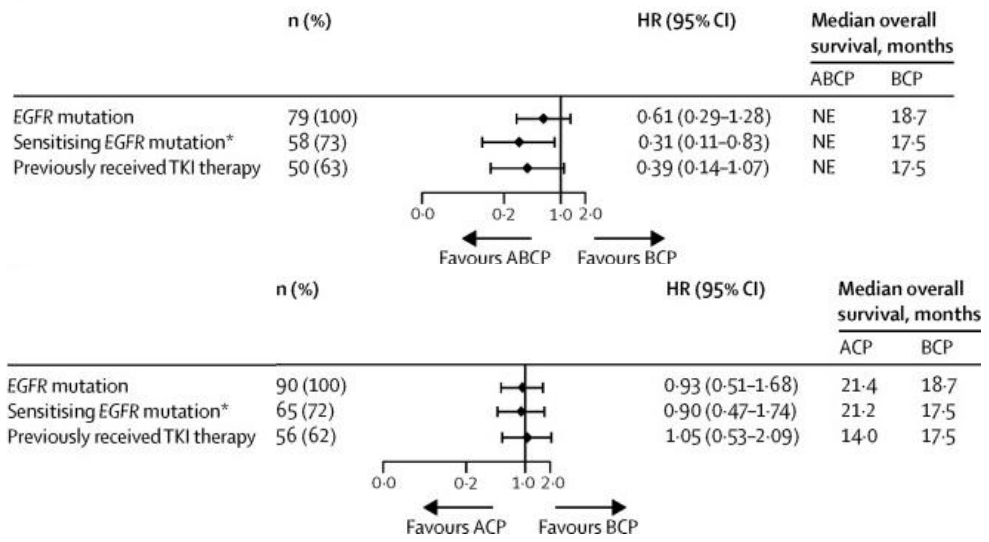
e) Checkpoint inhibitor as a single agent
   - Driver mutation – better response with EGFR inhibitor as above

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

Case Study 2

- This patient with cT4N3M1C SCC, PDL1 10% underwent Palliative Radiation 30Gy/10 fx to open up L mainstem bronchus f/b carbo/nab-paclitaxel/Pembrolizumab.
  - He is responding to therapy, clinically improving, now ambulating more with less SOB
- In the same patient who was a never-smoker, with AC, driver mutation and high PDL1 expression – thought provoking to differentiate between subgroups of NSCLC patients.