Memorial Sloan Kettering Cancer Center

ASCO 2020 Lung Cancer

Gregory J. Riely

June 2020

Disclosures

- MSK receives money for research conducted by me from:
  - Novartis
  - Pfizer
  - Merck
  - Mirati
  - Roche
  - Takeda

Highlights of ASCO 2020 (and other meetings)

- New, not particularly useful, data in small cell lung cancer
- The addition of a short course chemotherapy to combination immunotherapy for upfront treatment of patients with stage IV NSCLC without an oncogenic driver (“9LA”)
- MET exon 14 as a targetable oncogenic driver
- RET as a targetable oncogenic driver
- HER2 mutations as a targetable oncogenic driver
- EGFR targeted therapy in the adjuvant setting

Paradigm for treatment of Small Cell Lung Cancer Pre-2018

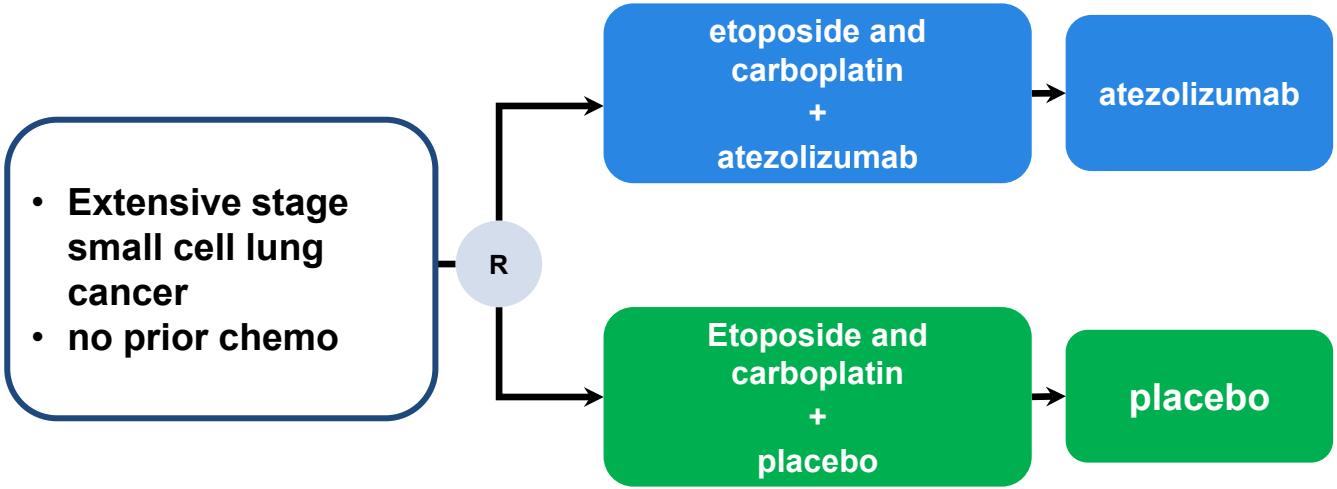
Platinum/etoposide
x 4-6 cycles

progression

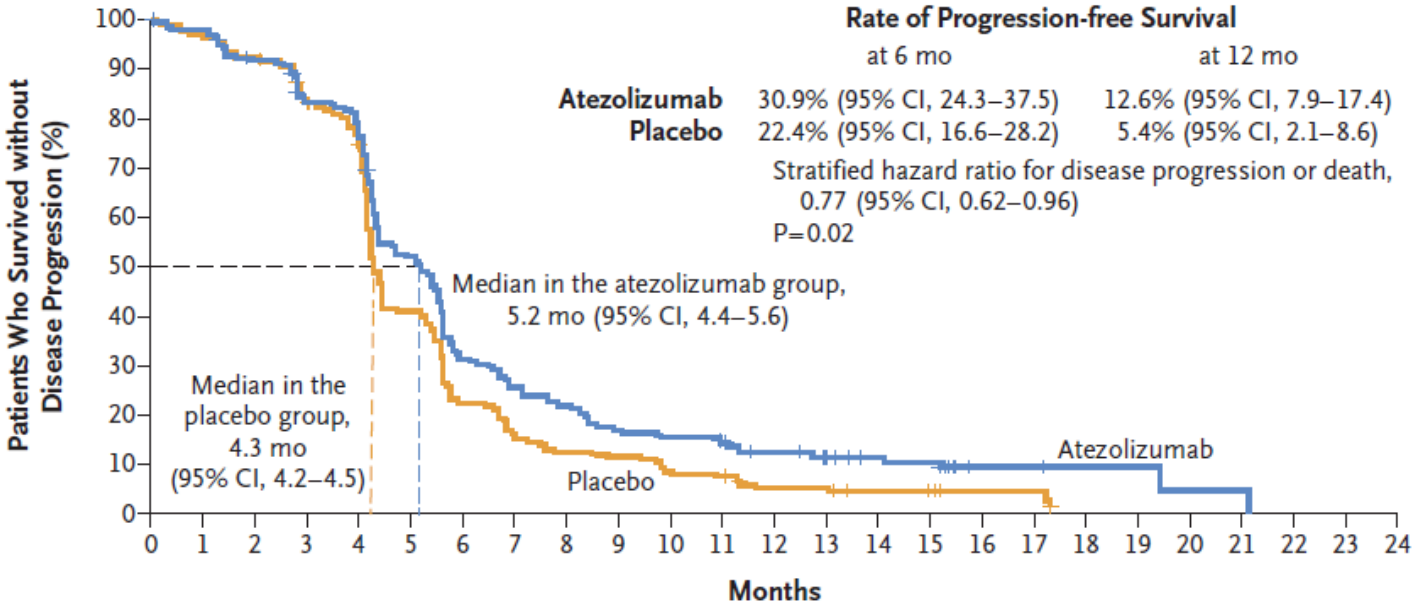
Topotecan

RR - 16%
median OS - 6–8 months

Evaluating Checkpoint Inhibitors in Patients with Small Cell Lung aCncer



Carboplatin/Etoposide +/- Atezolizumab: Progression-free survival



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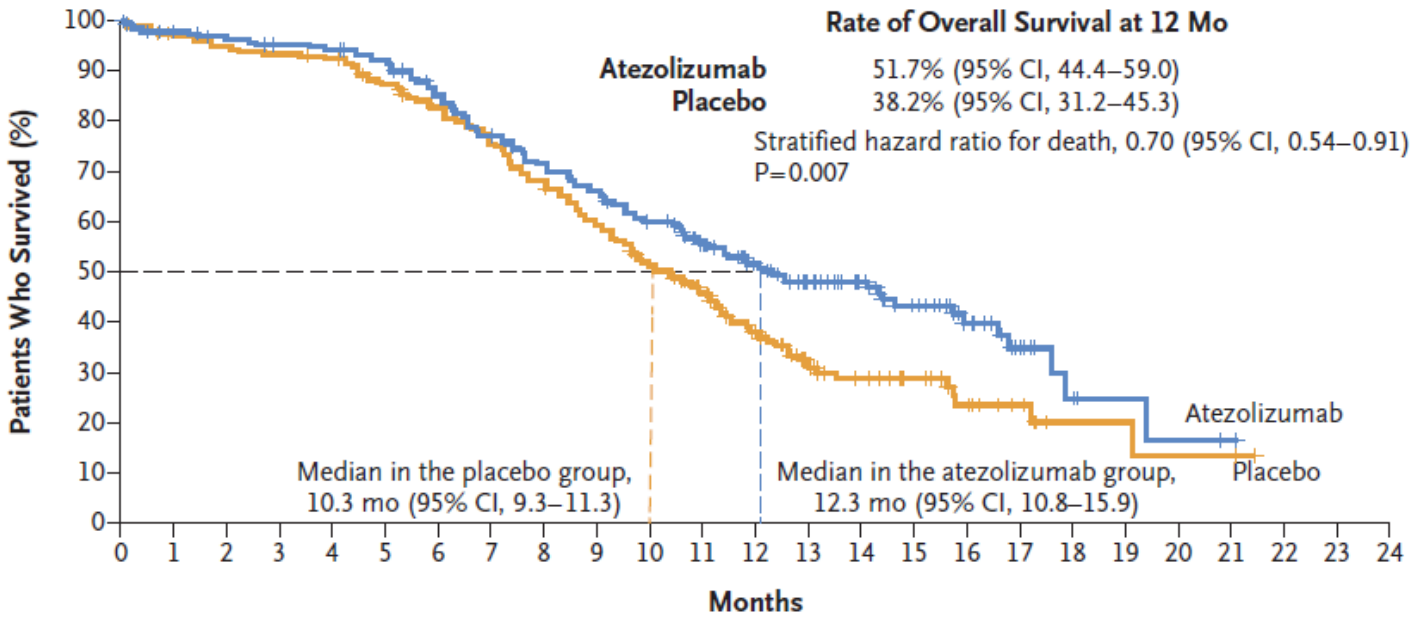
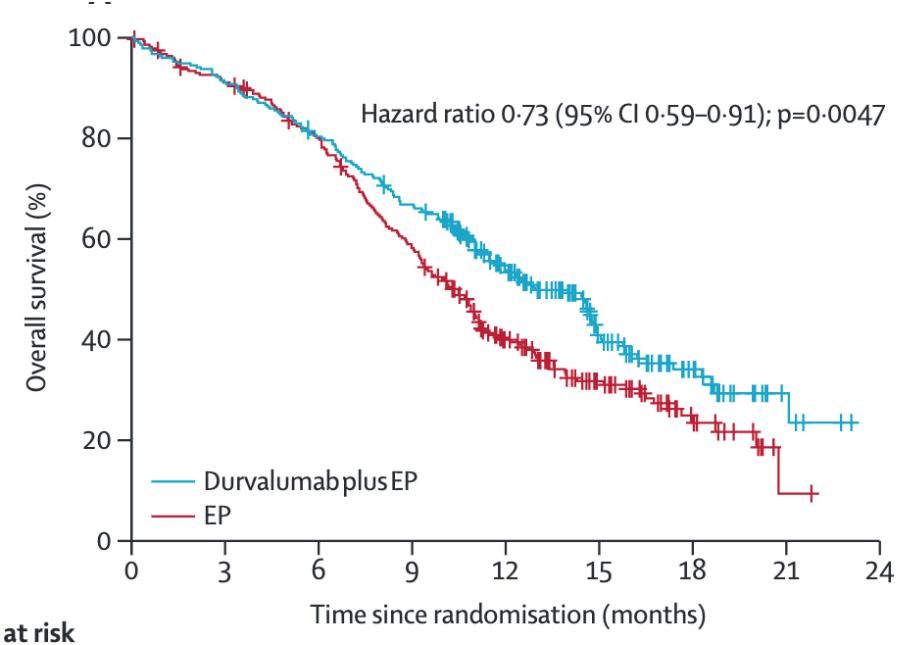
Horn et al, NEJM 2018.

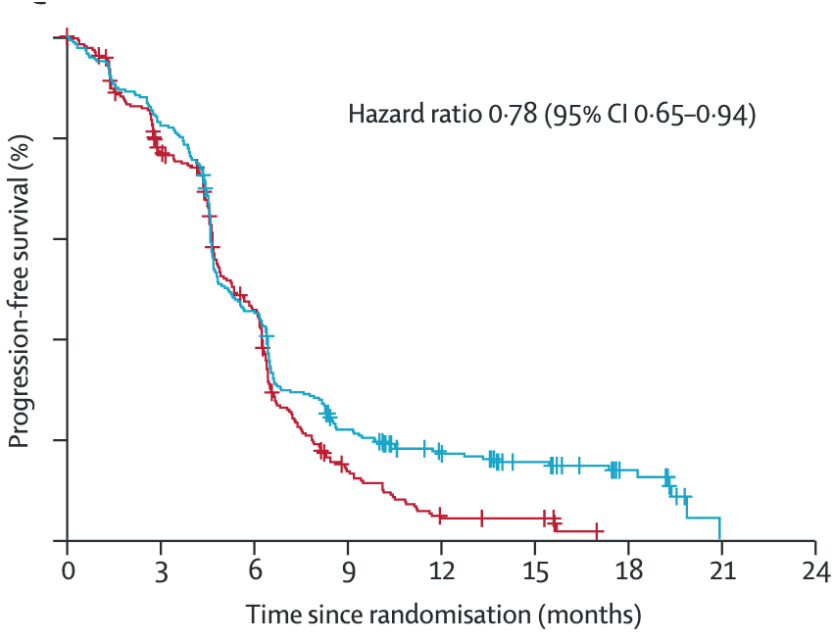
Carboplatin/Etoposide +/- Atezolizumab: Overall survival



Horn et al, NEJM 2018.

Platinum/etoposide +/- Durvalumab





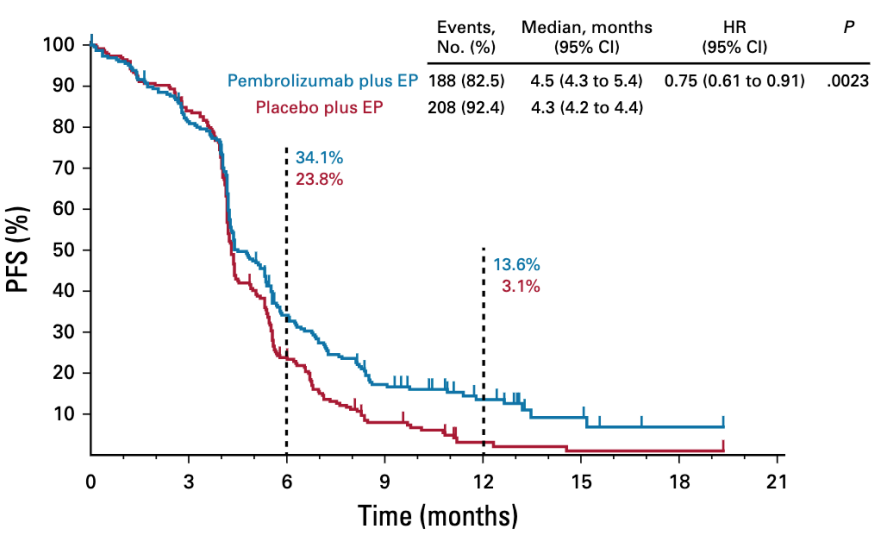
Number at risk

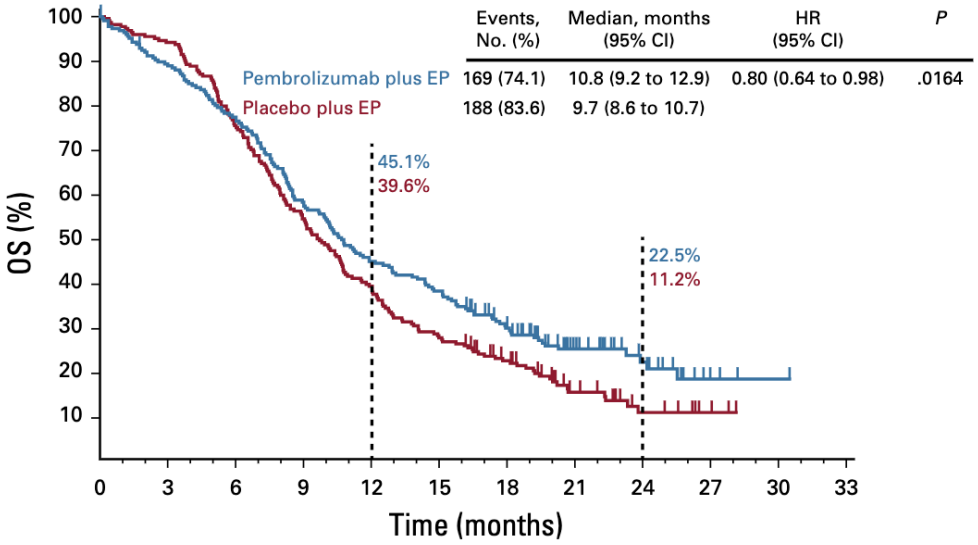
Durvalumab plus EP	268	244	214	177	116	57	25	5	0
EP	269	242	209	153	82	44	17	1	0

268	220	119	54	34	22	10	0	0
269	194	109	30	9	7	0	0	0

Paz-Ares, Lancet 2019

Platinum/Etoposide +/- Pembrolizumab in ES Small Cell





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Rudin et al ASCO 2020/JCO 2020

Since ASCO 2020

FDA grants accelerated approval to lurbinectedin for metastatic small cell lung cancer

June 15, 2020

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial

José Trigo, Vivek Subbiah*, Benjamin Besse, Victor Moreno, Rafael López, María Angeles Sala, Solange Peters, Santiago Ponce, Cristian Fernández, Vicente Alfaro, Javier Gómez, Carmen Kahatt, Ali Zeaiter, Khalil Zaman, Valentina Boni, Jennifer Arrondeau, Maite Martínez, Jean-Pierre Delord, Ahmad Awada, Rebecca Kristeleit, Maria Eugenia Olmedo, Luciano Wannesson, Javier Valdivia, María Jesús Rubio, Antonio Anton, John Sarantopoulos, Sant P Chawla, Joaquín Mosquera-Martinez, Manolo D'Arcangelo, Armando Santoro, Victor M Villalobos, Jacob Sands, Luis Paz-Ares*

Platinum/etoposide → progression → lurbinectidin

"a selective inhibitor of oncogenic transcription"

Caribbean sea squirt

Lurbinectedin as Second Line Therapy for Small Cell

	All Patients	Chemotherapy free interval <90 days	Chemotherapy free interval >90 days
Response Rate	35%	22%	45%
mDOR	5.3 months	4.7 months	6.2 months
mPFS	3.5 months	2.6 months	4.6 months
mOS	9.3 months	5.0 months	11.9 months

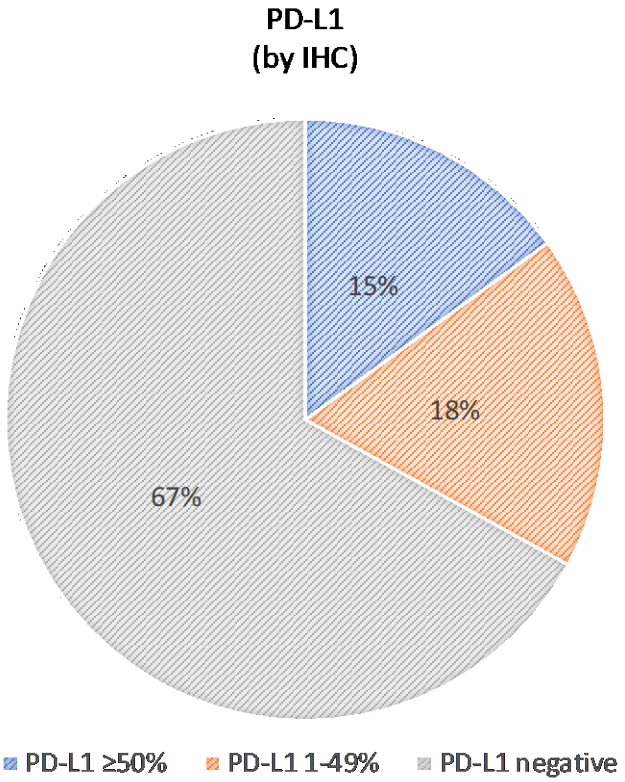
Trigo et al, Lancet Oncol 2020

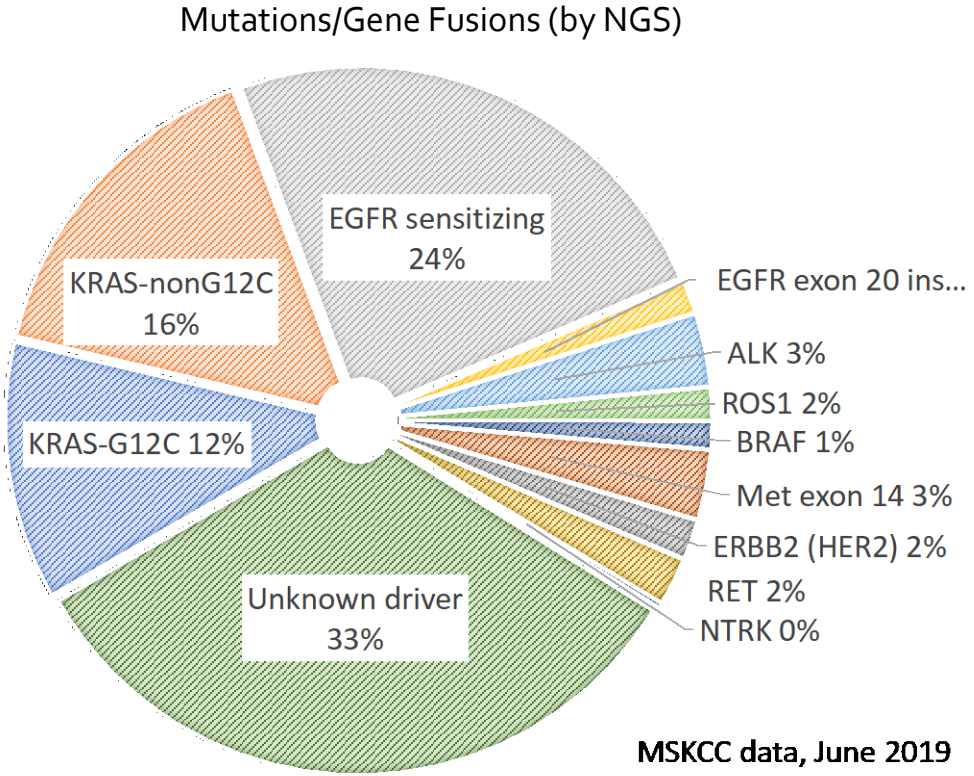
Summary of Small Cell Lung Cancer

- Standard first-line therapy is etoposide/platinum with an ICI. The anti-PD-1/PD-L1 antibodies FDA-approved in this setting are atezolizumab and durvalumab. Pembrolizumab and nivolumab have not shown positive phase III trials.

- Lurbinectedin is a new agent for treatment of patients with small cell lung cancer that has progressed after first-line therapy.

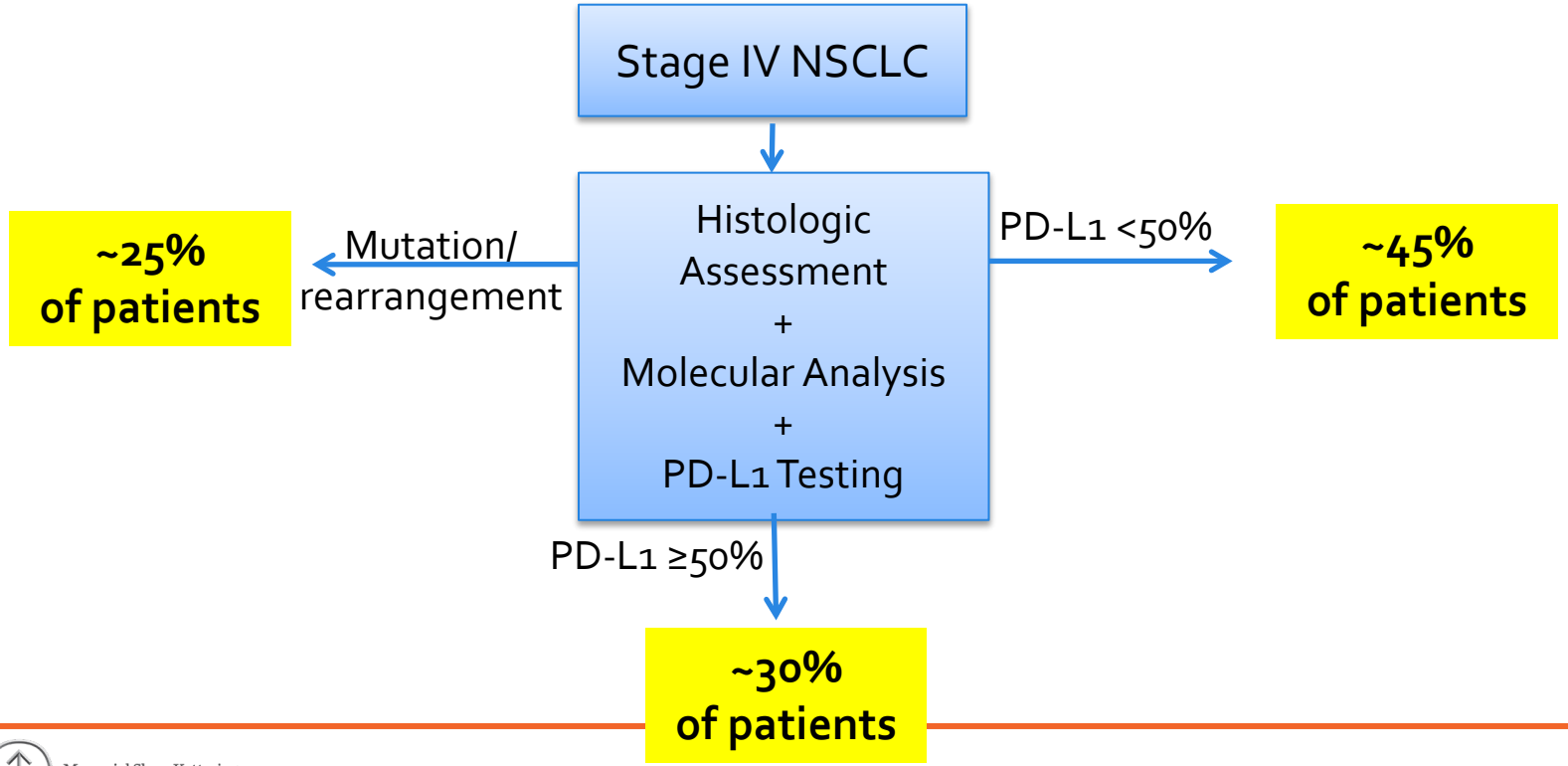
Classification of NSCLC by biomarkers



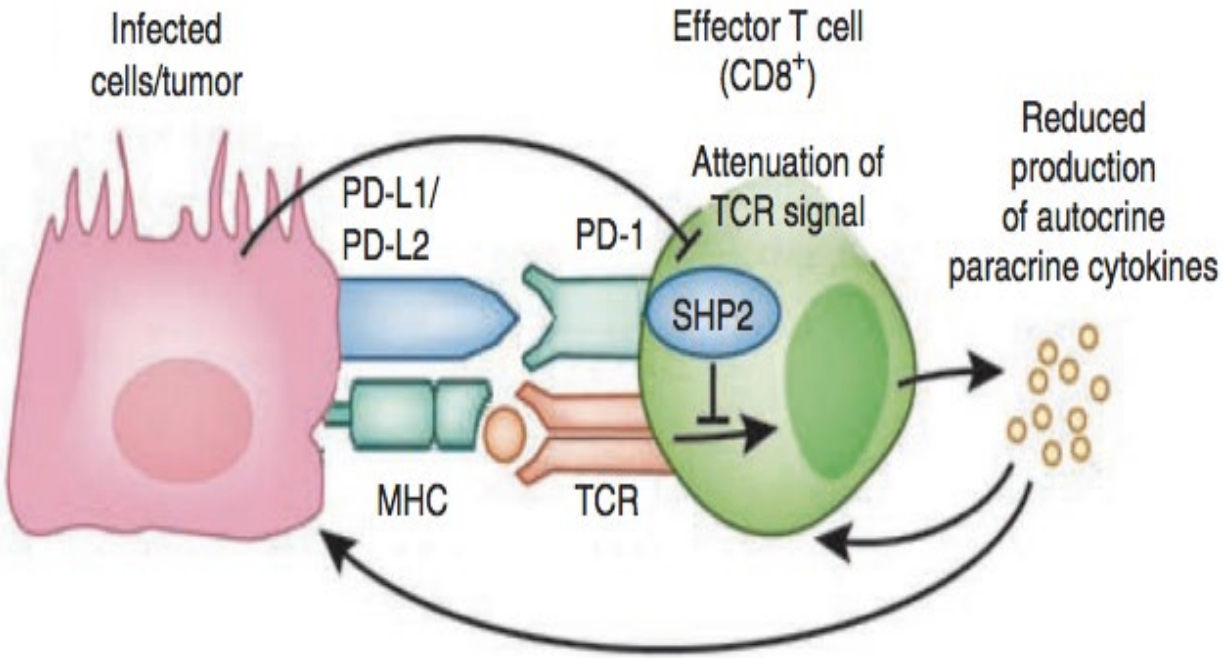


MSKCC data, June 2019

The Current Approach to First-Line Treatment of Patients with Advanced NSCLC

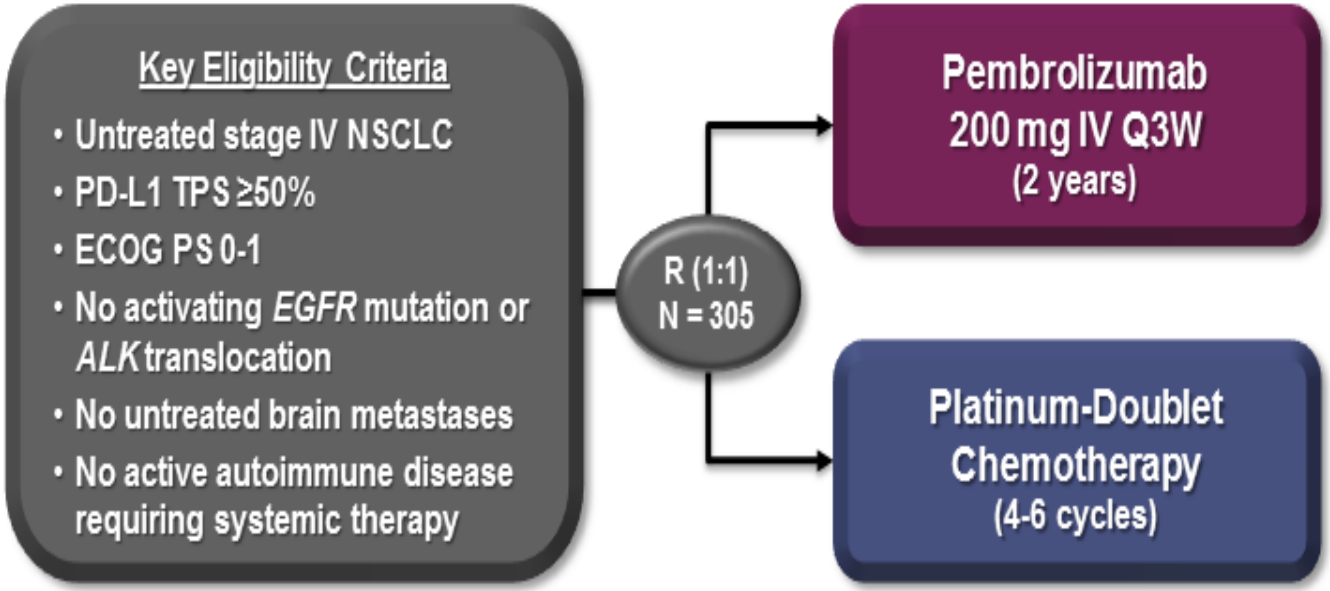


The Immunological Synapse



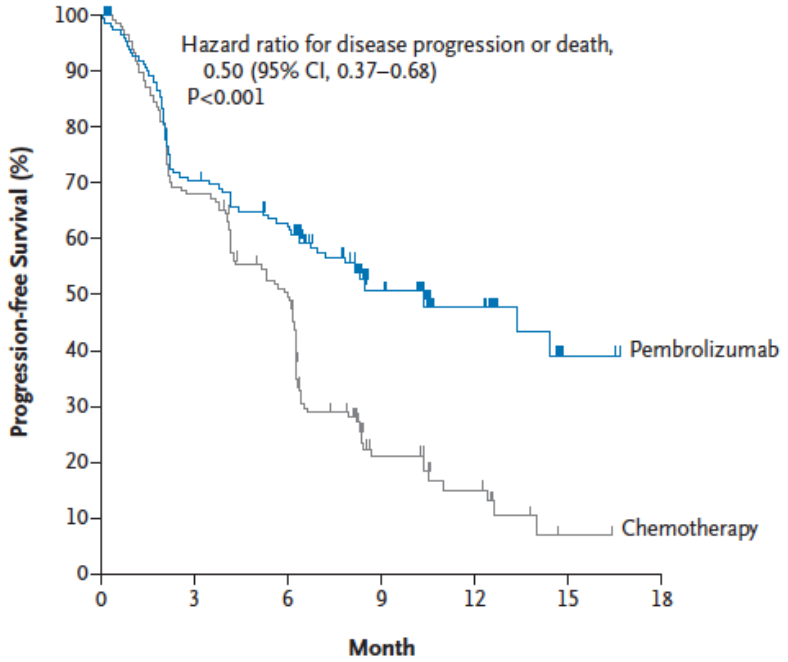
Okazaki et al, Nature Immunology 2013

Pembrolizumab vs Chemotherapy in Patients who are PD-L1 ≥ 50%



Reck et al, ESMO 2016

Pembrolizumab (anti-PD-1 Antibody) vs Chemotherapy in Patients who are PD-L1 ≥ 50%



Reck et al, NEJM 2016

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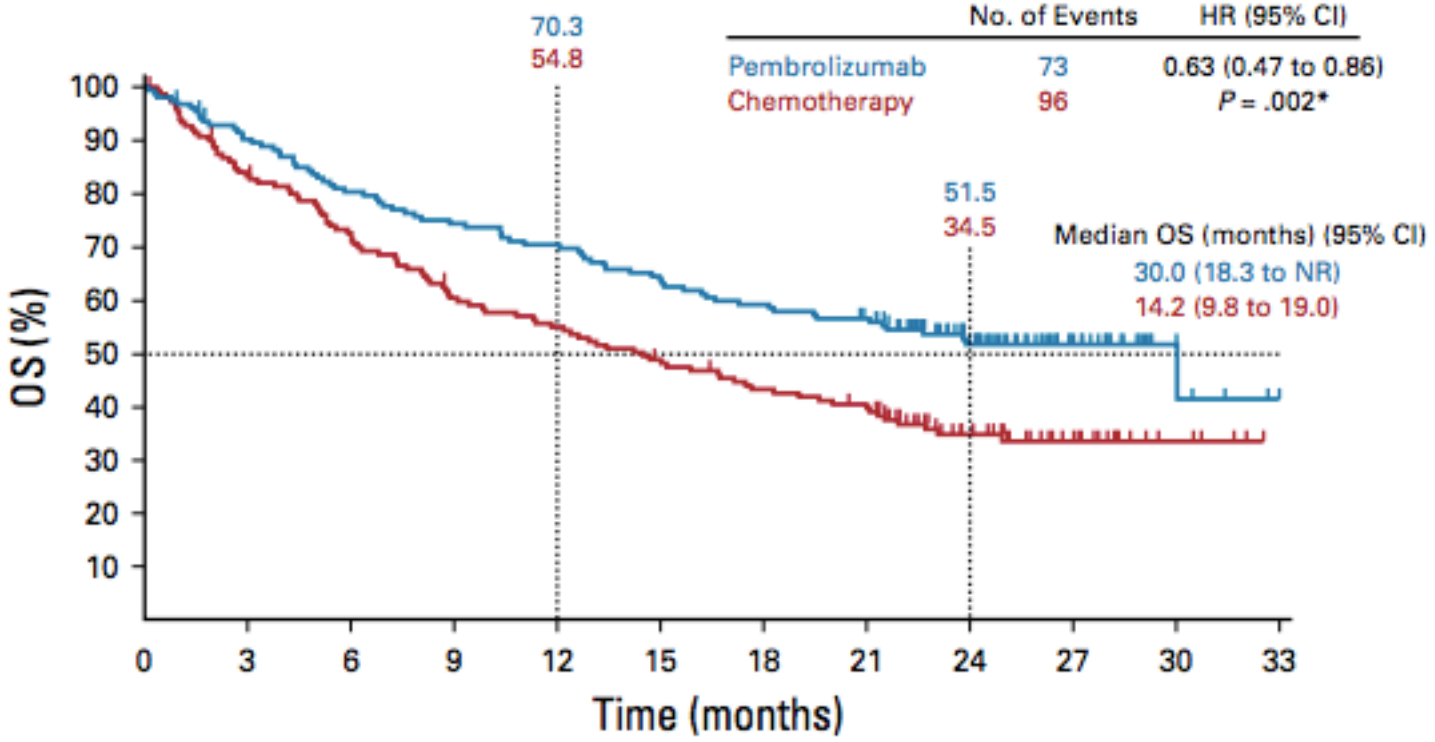

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Reck et al, JCO 2019

Pembrolizumab is Associated with Fewer Adverse Events than Chemotherapy

Adverse Event	Pembrolizumab Group (N=154)		Chemotherapy Group (N=150)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Treatment-related†				
Any	113 (73.4)	41 (26.6)	135 (90.0)	80 (53.3)
Serious	33 (21.4)	29 (18.8)	31 (20.7)	29 (19.3)
Led to discontinuation	11 (7.1)	8 (5.2)	16 (10.7)	9 (6.0)
Led to death	1 (0.6)	1 (0.6)	3 (2.0)	3 (2.0)
Occurred in ≥10% of patients in either group‡				
Nausea	15 (9.7)	0	65 (43.3)	3 (2.0)
Anemia	8 (5.2)	3 (1.9)	66 (44.0)	29 (19.3)
Fatigue	16 (10.4)	2 (1.3)	43 (28.7)	5 (3.3)
Decreased appetite	14 (9.1)	0	39 (26.0)	4 (2.7)
Diarrhea	22 (14.3)	6 (3.9)	20 (13.3)	2 (1.3)
Neutropenia	1 (0.6)	0	34 (22.7)	20 (13.3)
Vomiting	4 (2.6)	1 (0.6)	30 (20.0)	1 (0.7)
Pyrexia	16 (10.4)	0	8 (5.3)	0

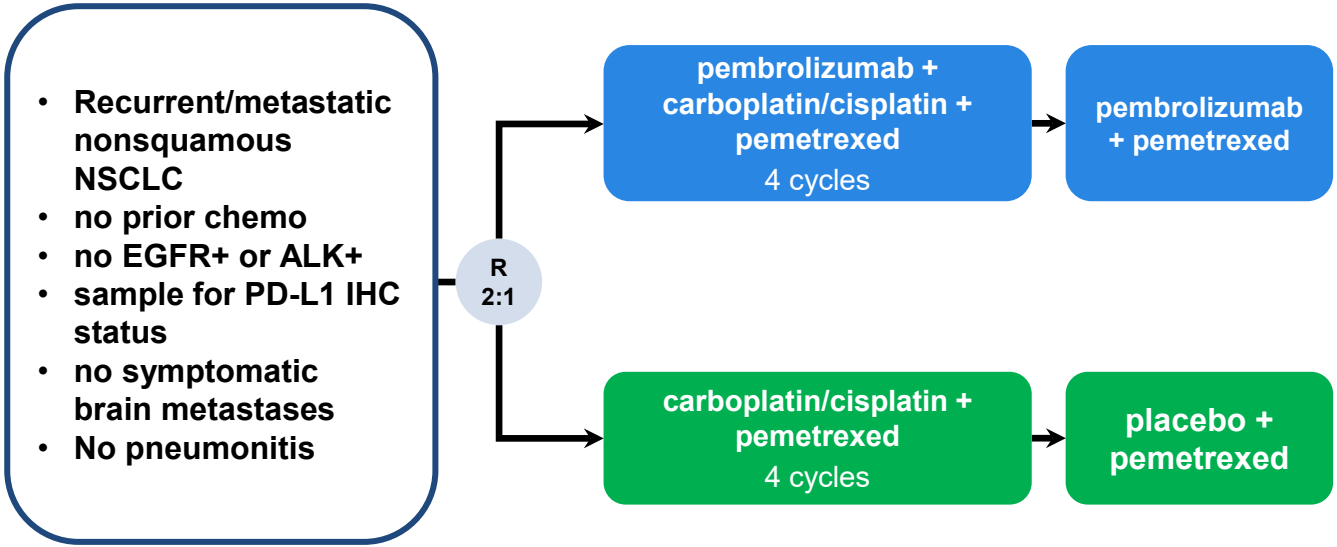
Reck et al, NEJM 2016

There are Immune-Related Adverse Events

Adverse Event	Pembrolizumab Group (N=154)		Chemotherapy Group (N=150)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Immune-mediated‖				
Any	45 (29.2)	15 (9.7)	7 (4.7)	1 (0.7)
Hypothyroidism	14 (9.1)	0	2 (1.3)	0
Hyperthyroidism	12 (7.8)	0	2 (1.3)	0
Pneumonitis	9 (5.8)	4 (2.6)	1 (0.7)	1 (0.7)
Infusion reaction	7 (4.5)	0	2 (1.3)	0
Severe skin reaction	6 (3.9)	6 (3.9)	0	0
Thyroiditis	4 (2.6)	0	0	0
Colitis	3 (1.9)	2 (1.3)	0	0
Myositis	3 (1.9)	0	0	0
Hypophysitis	1 (0.6)	1 (0.6)	0	0
Nephritis	1 (0.6)	1 (0.6)	0	0
Pancreatitis	1 (0.6)	1 (0.6)	0	0
Type 1 diabetes mellitus	1 (0.6)	1 (0.6)	0	0

Reck et al, NEJM 2016

Randomized Trial of Chemotherapy +/- Pembrolizumab in “non-squamous” NSCLC



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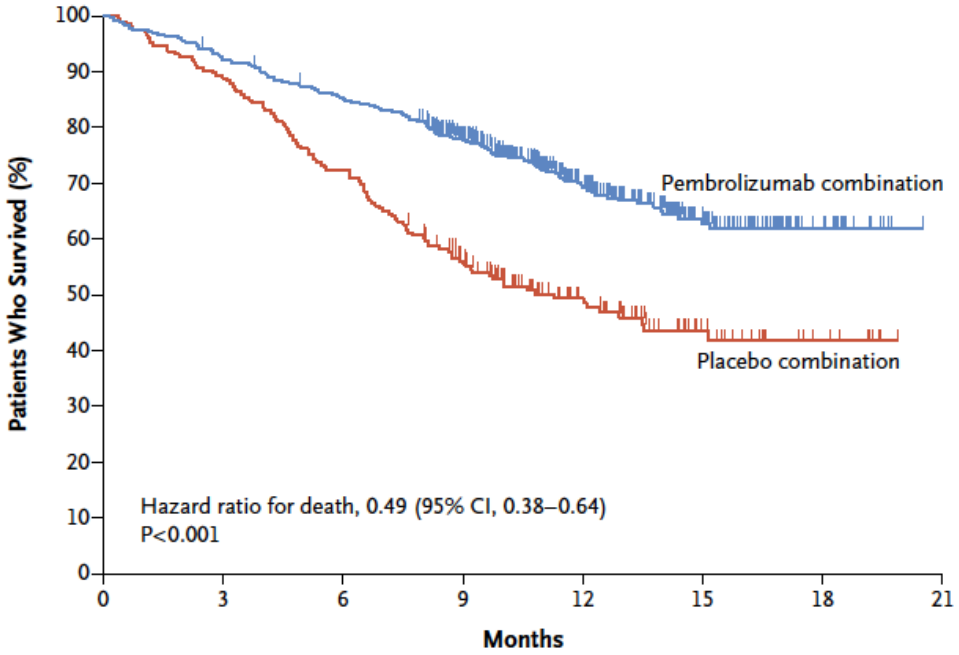
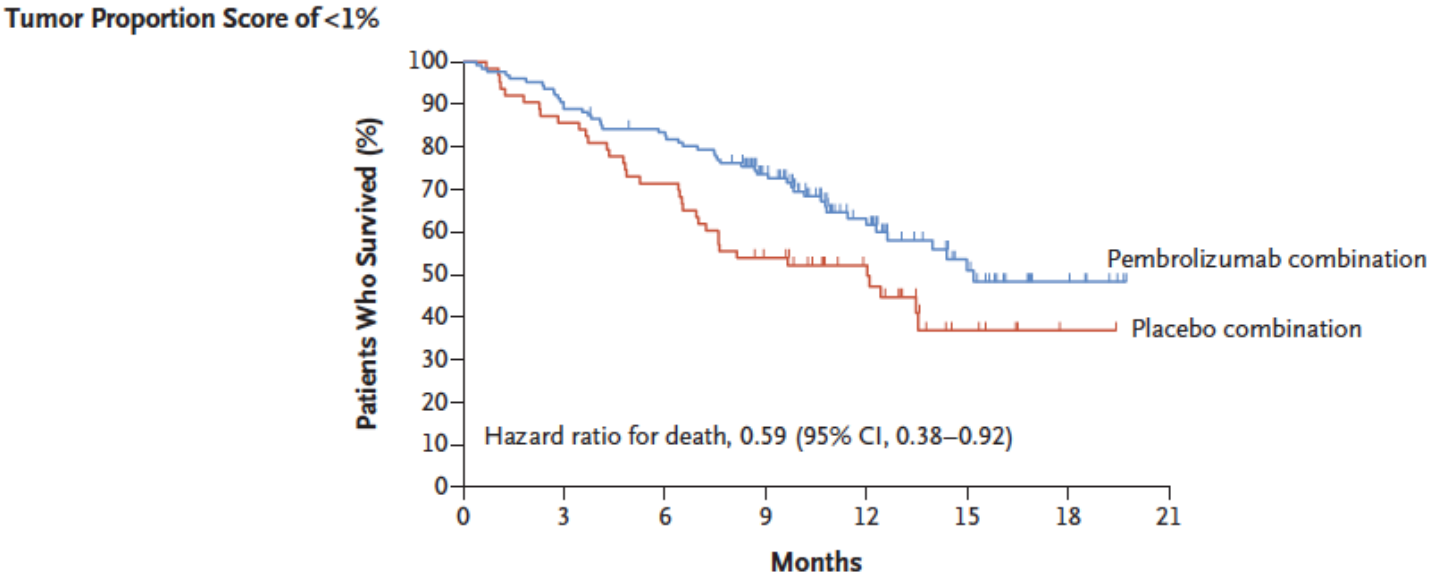


Gandhi et al NEJM 2018

Randomized Trial of Chemotherapy +/- Pembrolizumab in “non-squamous” NSCLC



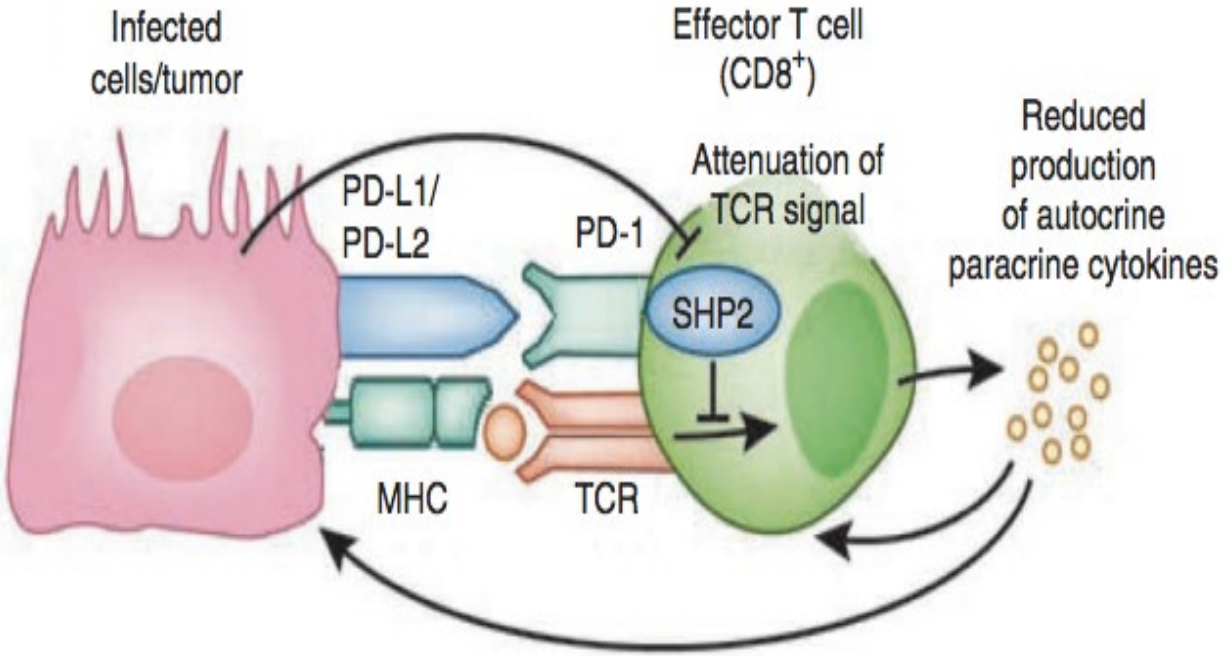
Gandhi et al NEJM 2018

Chemotherapy + Immunotherapy for NSCLC

	Histology	Improved PFS?	Improved OS?
Carboplatin, pemetrexed, pembrolizumab	Non-squam	Yes	Yes
Carboplatin, paclitaxel, bevacizumab, atezolizumab	Non-squam	Yes	Yes
Carboplatin, nab-paclitaxel, atezolizumab	Non-squam	Yes	Yes
Carboplatin, taxane, pembrolizumab	Squamous	Yes	Yes

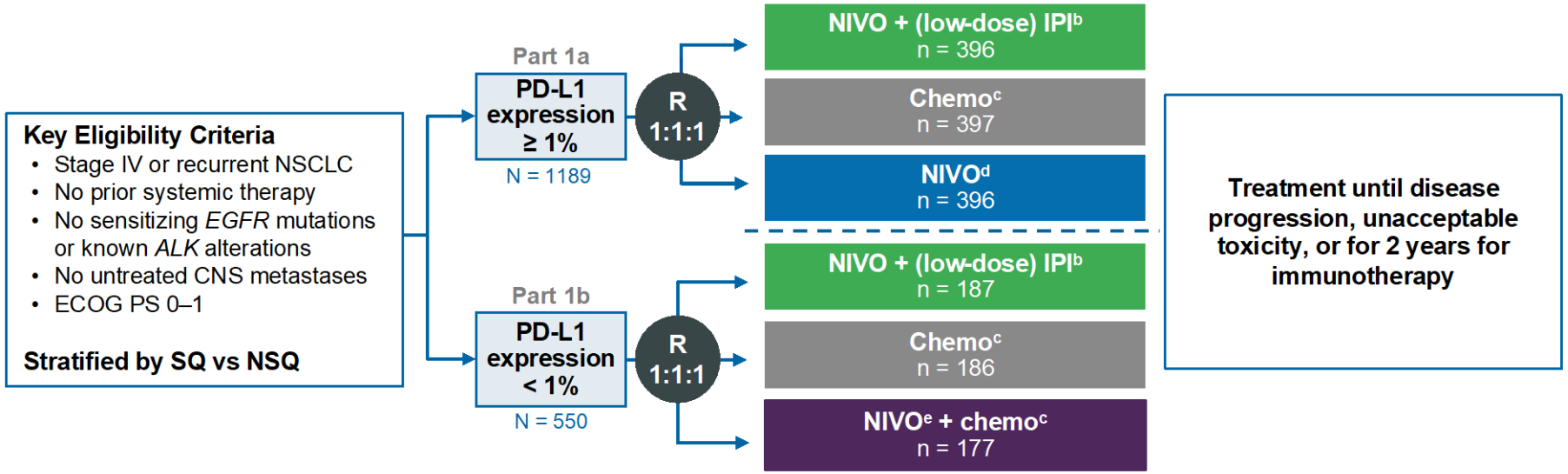
Gandhi et al, NEJM 2018; Socinski et al, NEJM 2018; West et al, Lancet Onc 2019; Paz-Ares, NEJM 2018

What about checkpoint inhibitor combinations?



Okazaki et al, Nature Immunology 2013

Exploring Ipi/Nivo combo instead of chemotherapy+IO



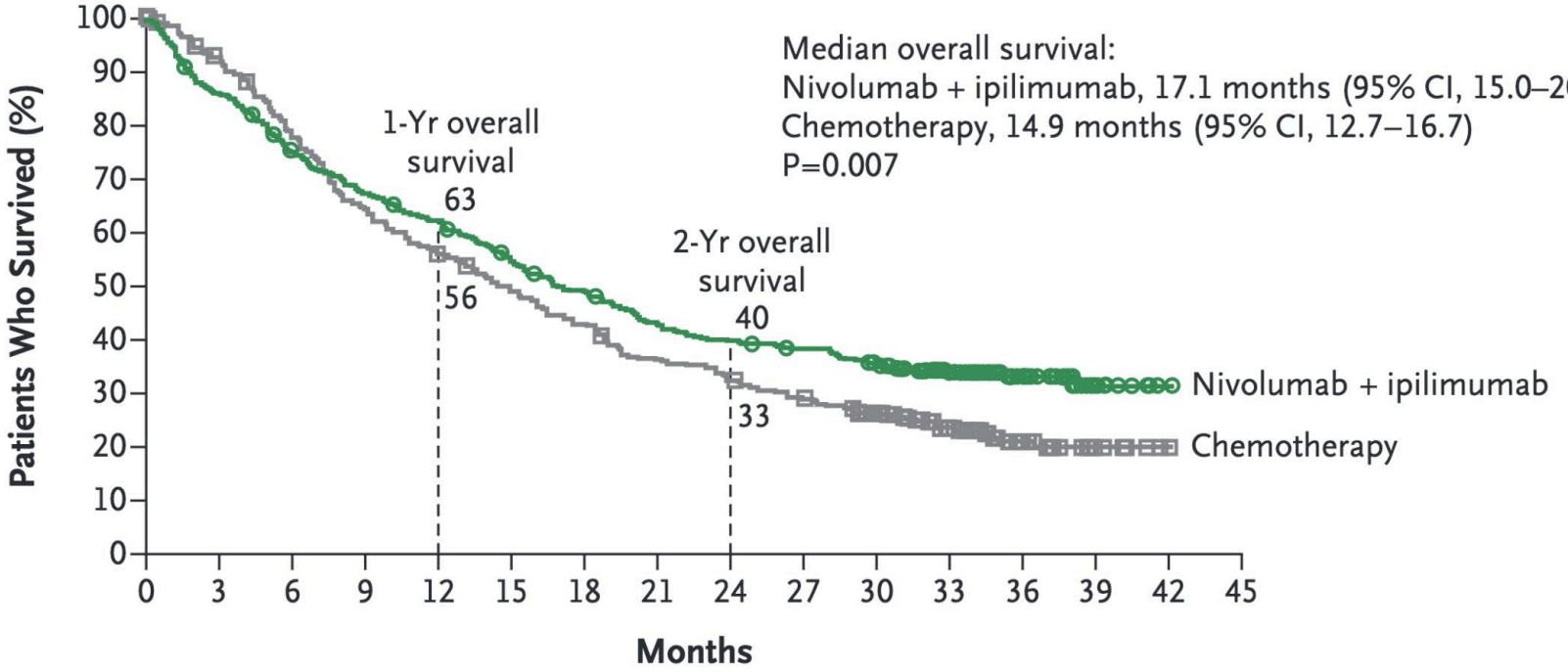
Independent co-primary endpoints: NIVO + IPI vs chemo
- PFS in high TMB populations[f]
- OS in PD-L1 ≥ 1% populations[g]

Secondary endpoints (PD-L1 hierarchy):
- PFS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO vs chemo** in PD-L1 ≥ 50%

Adapted from Peters et al, ESMO 2019

Ipi/Nivo improved OS compared with chemotherapy (w/o anti-PD-(L)1 Ab) in PD-L1 positive

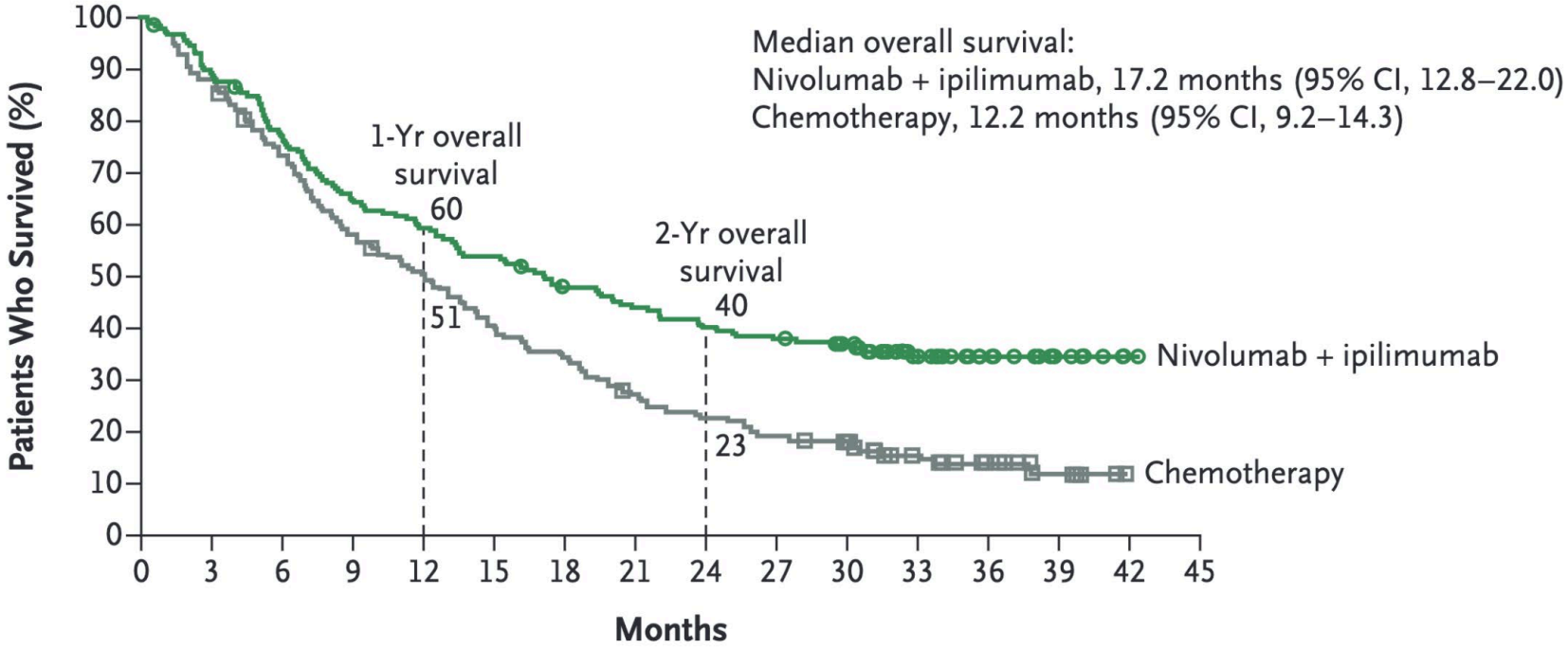
Overall Survival in Patients with a PD-L1 Expression Level of 1% or More



Hellmann et al, NEJM 2019

Ipi/Nivo improved OS compared with chemotherapy (w/o anti-PD-(L)1 Ab) in PD-L1 negative

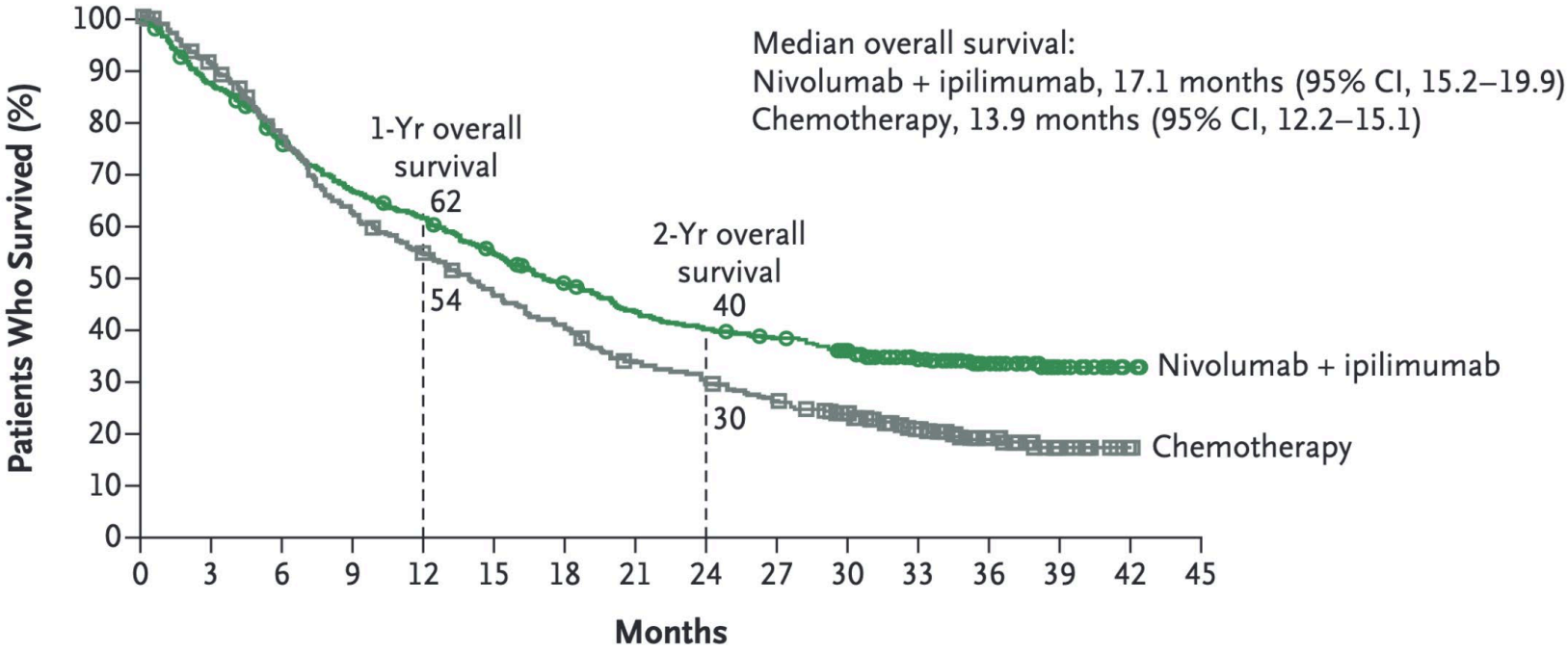
Overall Survival in Patients with a PD-L1 Expression Level of <1%



Hellmann et al, NEJM 2019

Ipi/Nivo improved OS compared with chemotherapy (w/o anti-PD-(L)1 Ab) regardless of PD-L1 status

Overall Survival in All the Patients



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Hellmann et al, NEJM 2019

The caveat… less chemo doesn't mean less tox

Adverse Event	Nivolumab plus Ipilimumab (N=576)		Chemotherapy (N=570)	
	Any Grade	Grade 3–4	Any Grade	Grade 3–4
	number of patients (percent)			
Treatment-related adverse events				
All events	442 (76.7)	189 (32.8)	467 (81.9)	205 (36.0)
Reported in ≥15% of patients				
Diarrhea	98 (17.0)	10 (1.7)	55 (9.6)	4 (0.7)
Rash	98 (17.0)	9 (1.6)	30 (5.3)	0
Fatigue	83 (14.4)	10 (1.7)	108 (18.9)	8 (1.4)
Decreased appetite	76 (13.2)	4 (0.7)	112 (19.6)	7 (1.2)
Nausea	57 (9.9)	3 (0.5)	206 (36.1)	12 (2.1)
Anemia	22 (3.8)	8 (1.4)	188 (33.0)	66 (11.6)
Neutropenia	1 (0.2)	0	98 (17.2)	54 (9.5)
Treatment-related serious adverse events	141 (24.5)	106 (18.4)	79 (13.9)	61 (10.7)
Treatment-related adverse events leading to discontinuation†	104 (18.1)	71 (12.3)	52 (9.1)	28 (4.9)

Hellmann et al, NEJM 2019

So, our options…

PD-L1	
High (TPS > 50%, TC3/IC3)	pembrolizumab atezolizumab
Low (TPS >1%)	pembrolizumab
Any	carboplatin, pemetrexed, pembrolizumab* carboplatin, paclitaxel, pembrolizumab carboplatin, nab-paclitaxel, atezolizumab* carboplatin, paclitaxel, bevacizumab, atezolizumab* ipilimumab, nivolumab

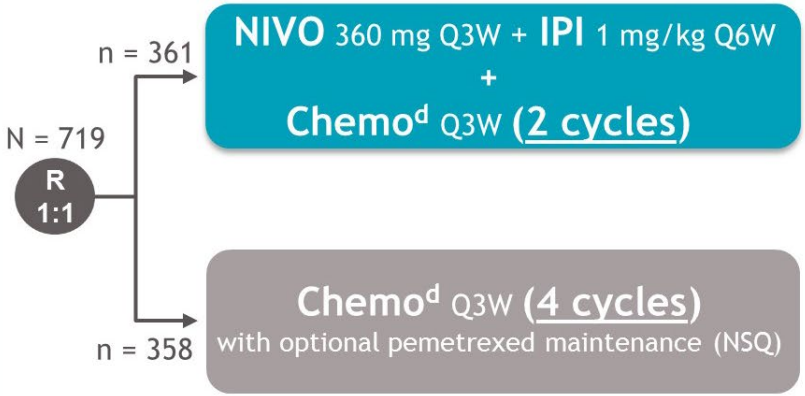
*regimens for non-squamous NSCLC

Studying chemotherapy + ipilimumab/nivolumab

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)



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

Primary endpoint
- OS

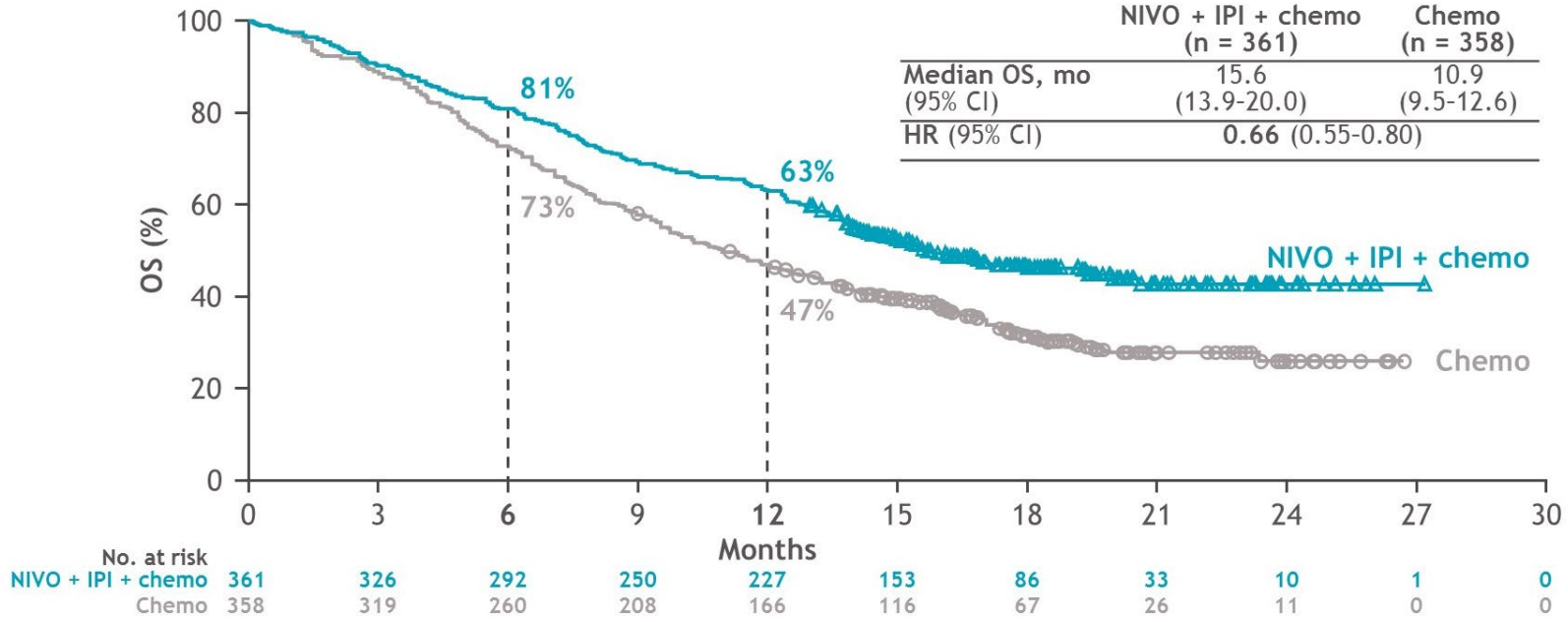
Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

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

Studying chemotherapy + ipilimumab/nivolumab Overall Survival



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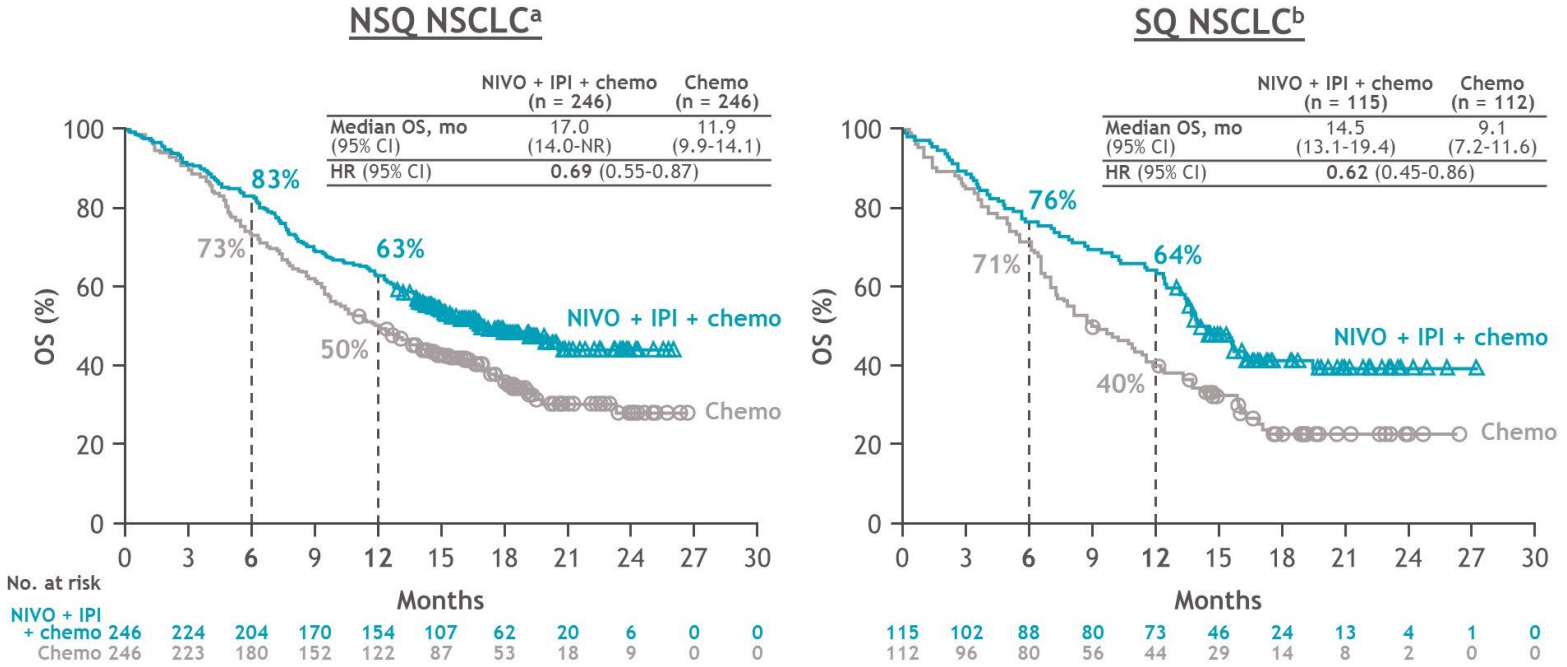
Reck et al, ASCO 2020

Studying chemotherapy + ipilimumab/nivolumab Overall Survival

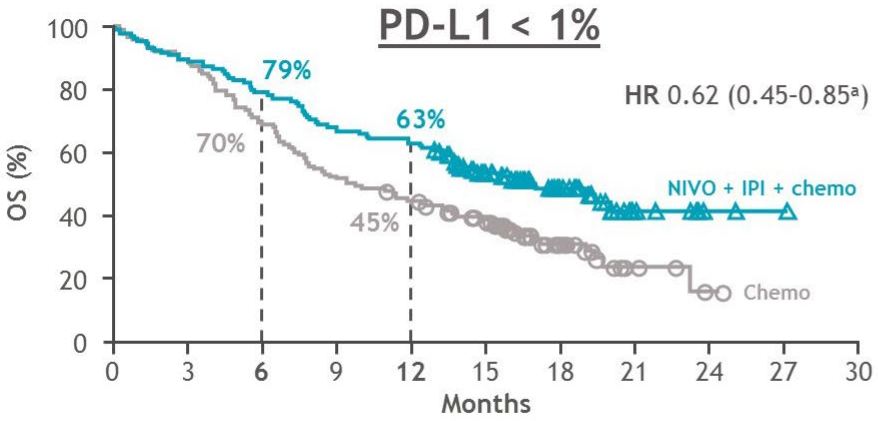


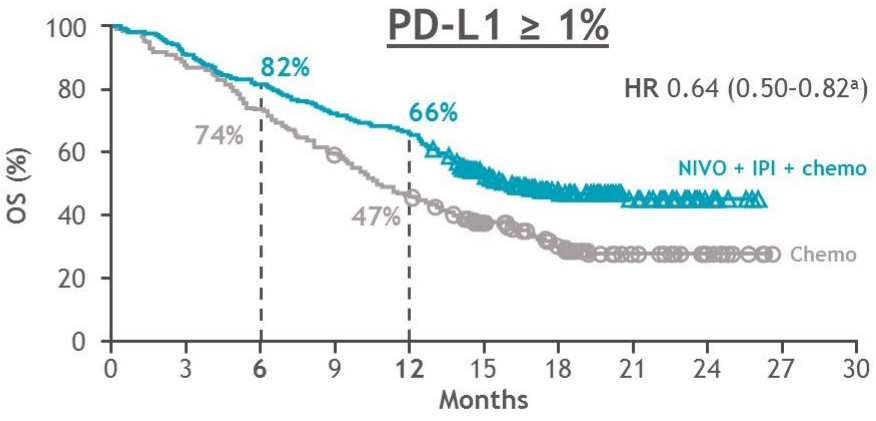
Minimum follow-up: 12.7 months.

[a]Subsequent systemic therapy was received by 30% of patients in the NIVO + IPI + chemo arm and 39% of patients in the chemo arm; subsequent immunotherapy was received by 6% and 28%, and subsequent chemotherapy by 29% and 22%, respectively; [b]Subsequent systemic therapy was received by 31% of patients in the NIVO + IPI + chemo arm and 44% of patients in the chemo arm; subsequent immunotherapy was received by 4% and 35%, and subsequent chemotherapy by 30% and 24% of patients, respectively

Reck et al, ASCO 2020

Studying chemotherapy + ipilimumab/nivolumab Overall Survival by PD-L1 status



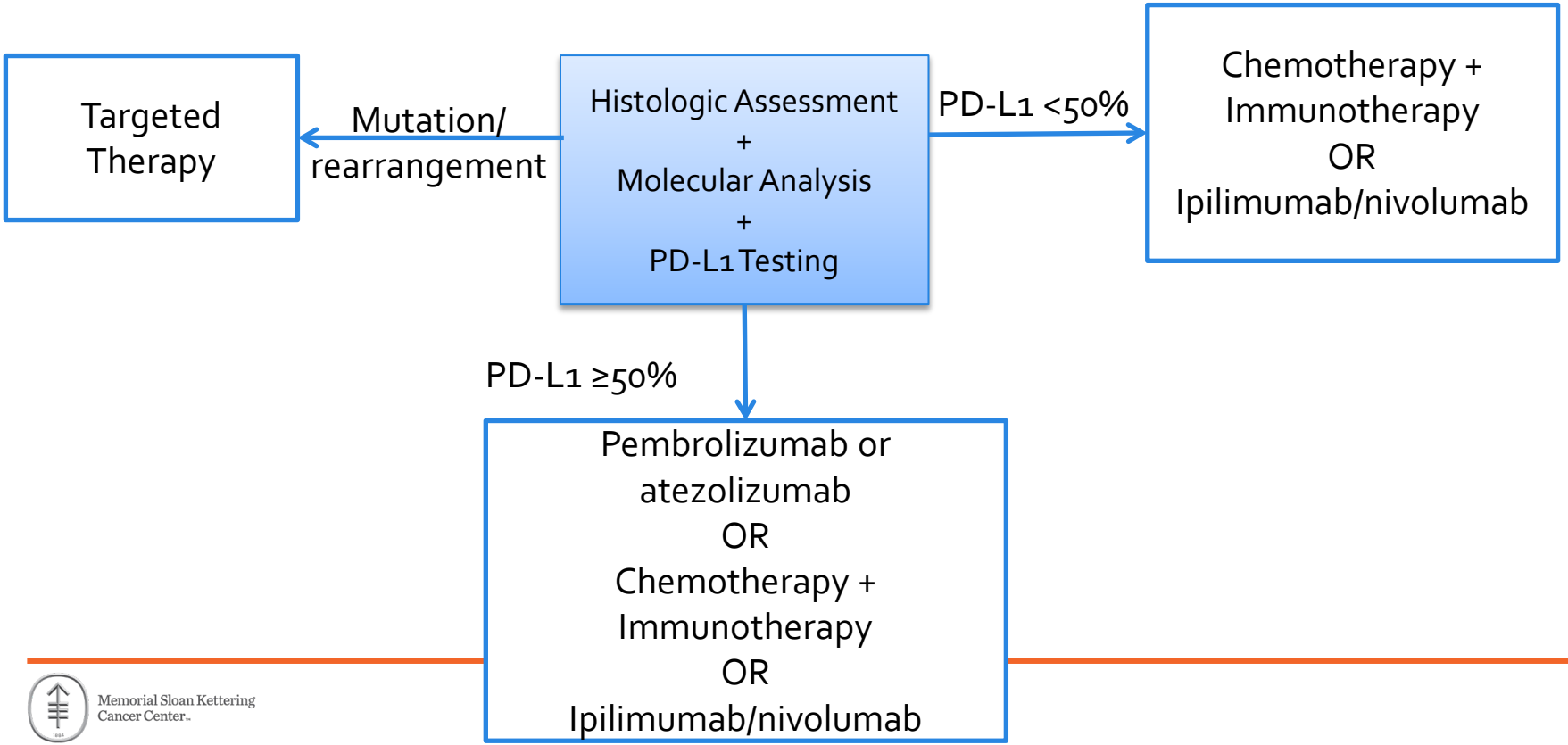


Reck et al, ASCO 2020

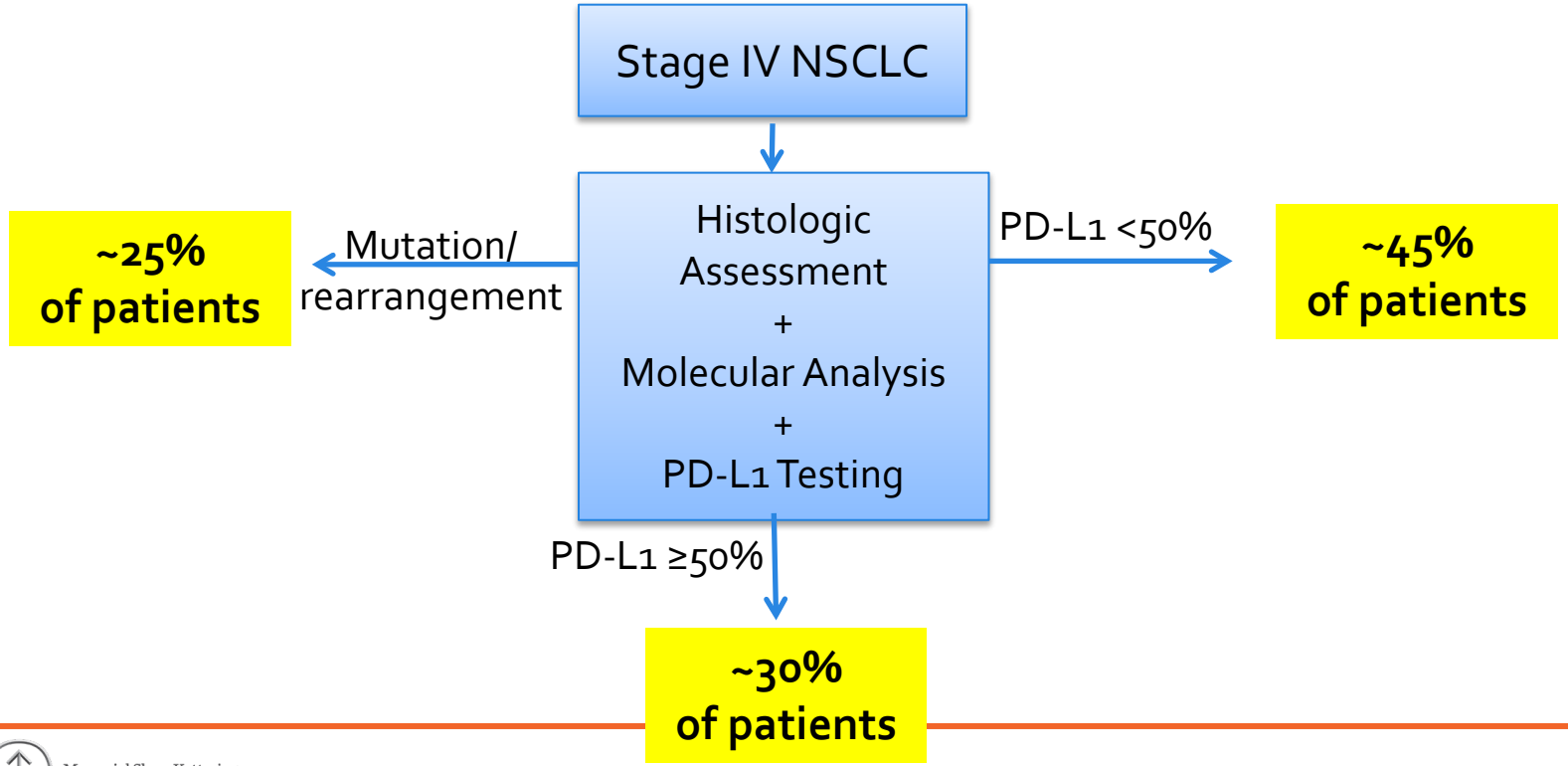
So, our options…

PD-L1	
High (> 50%, TC3/IC3)	pembrolizumab atezolizumab
Low (TPS >1%)	pembrolizumab
Any (squamous)	carboplatin, paclitaxel, pembrolizumab ipilimumab/nivolumab carboplatin paclitaxel, ipilimumab/nivolumab
Any (non-squamous)	carboplatin, pemetrexed, pembrolizumab carboplatin, paclitaxel, bevacizumab, atezolizumab carboplatin, nab-paclitaxel, atezolizumab ipilimumab/nivolumab carboplatin, pemetrexed, ipilimumab/nivolumab

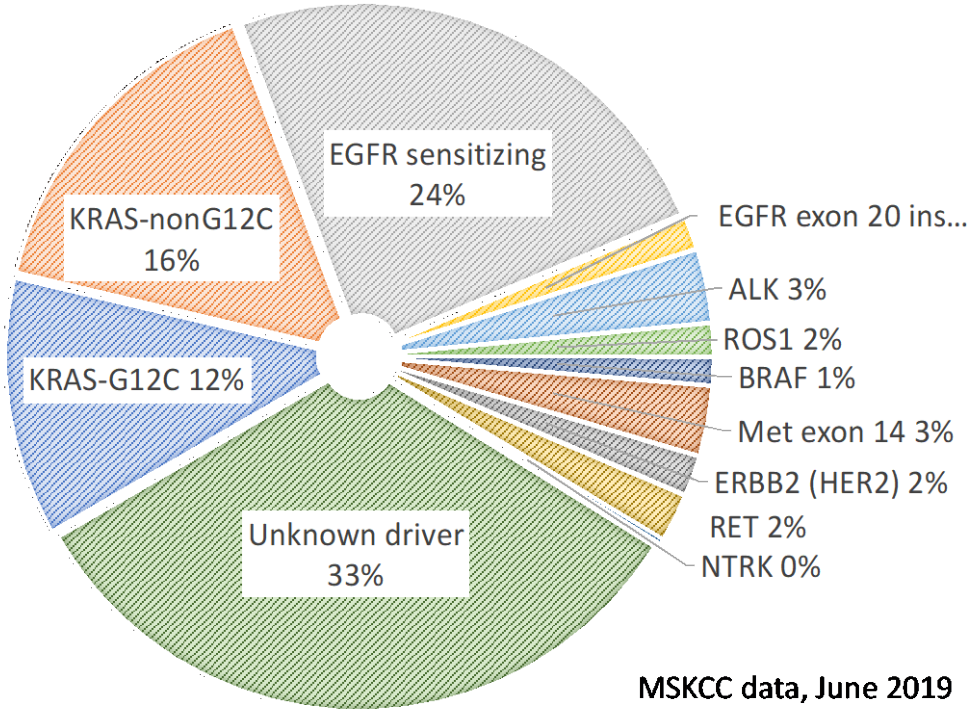
The Current Approach to First-Line Treatment of Patients with Advanced NSCLC



The Current Approach to First-Line Treatment of Patients with Advanced NSCLC



Molecular Subtypes of Lung Cancer

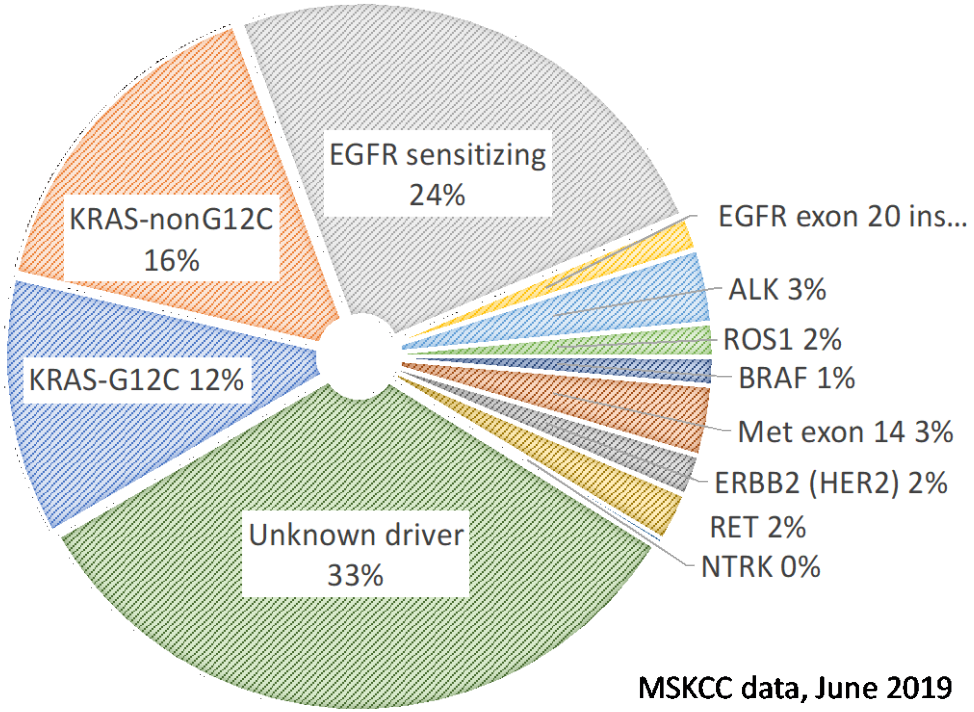


MSKCC data, June 2019

Key Subtypes

EGFR
ALK
ROS1
BRAF
NTRK

Molecular Subtypes of Lung Cancer

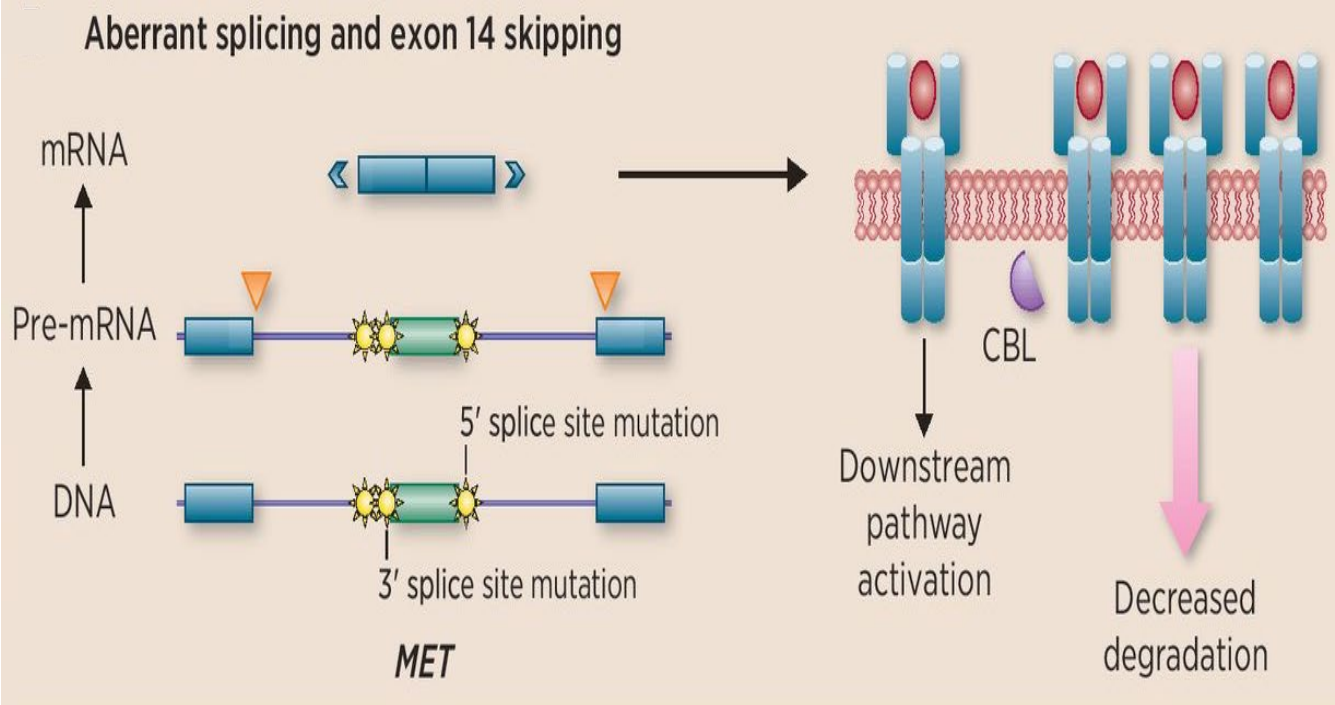


MSKCC data, June 2019

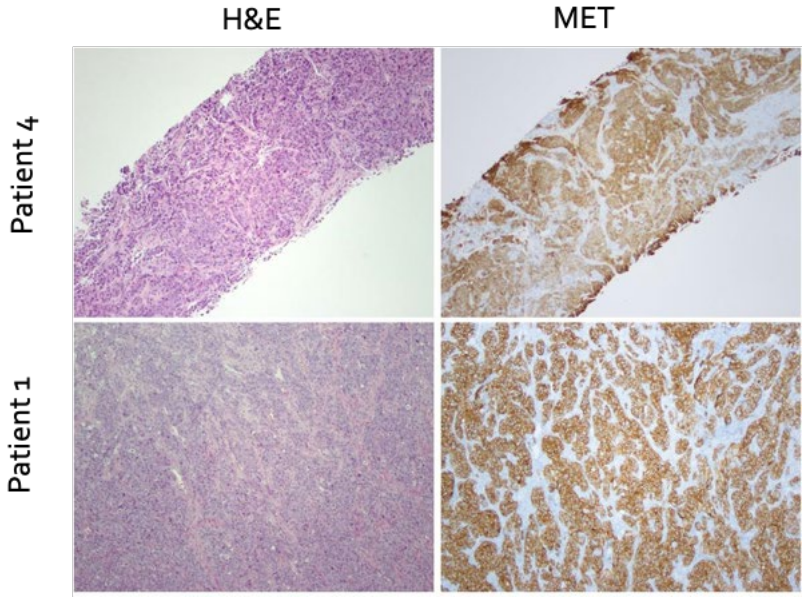
Key Subtypes

EGFR
ALK
ROS1
BRAF
NTRK
MET exon 14
RET

MET Exon 14 Alterations in NSCLC

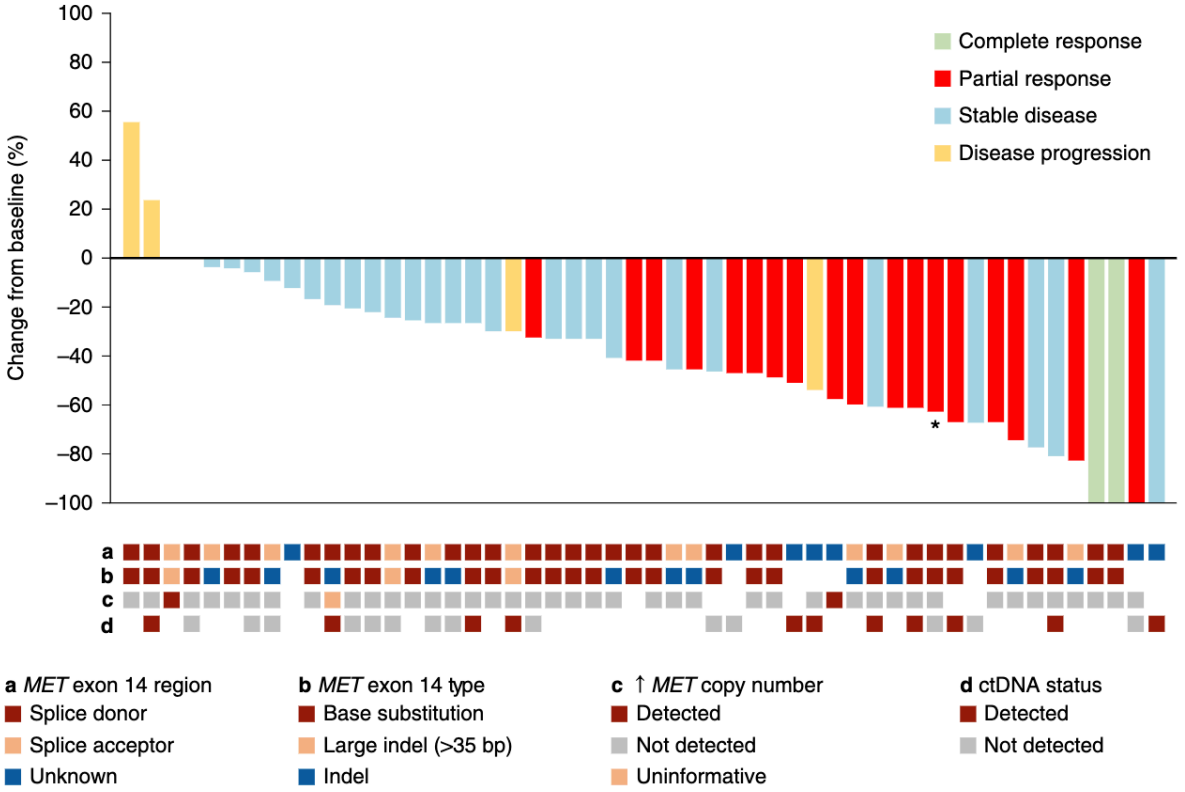


MET exon 14 alterations are associated with high MET expression



Paik et al, ASCO 2015

Crizotinib in Patients with MET Exon 14 Altered NSCLC



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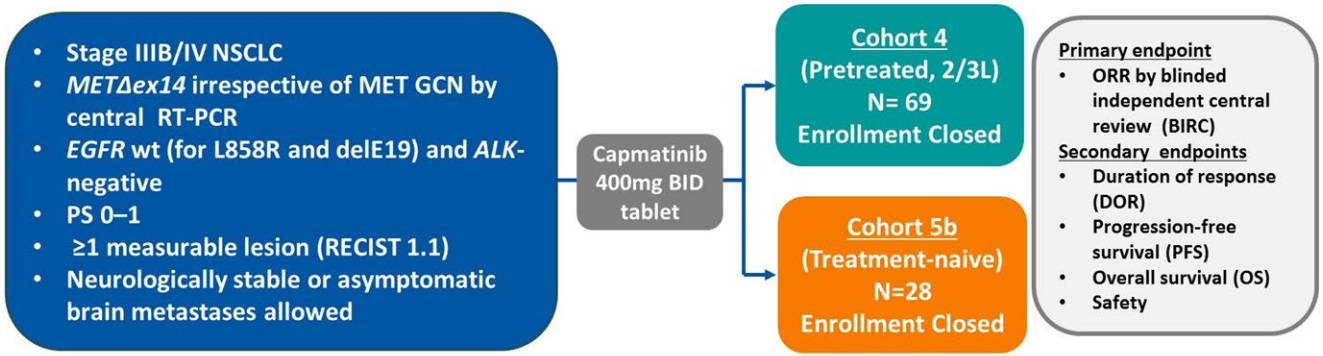
Drilon et al, Nature Medicine 2020

Capmatinib in MET exon 14 skipping



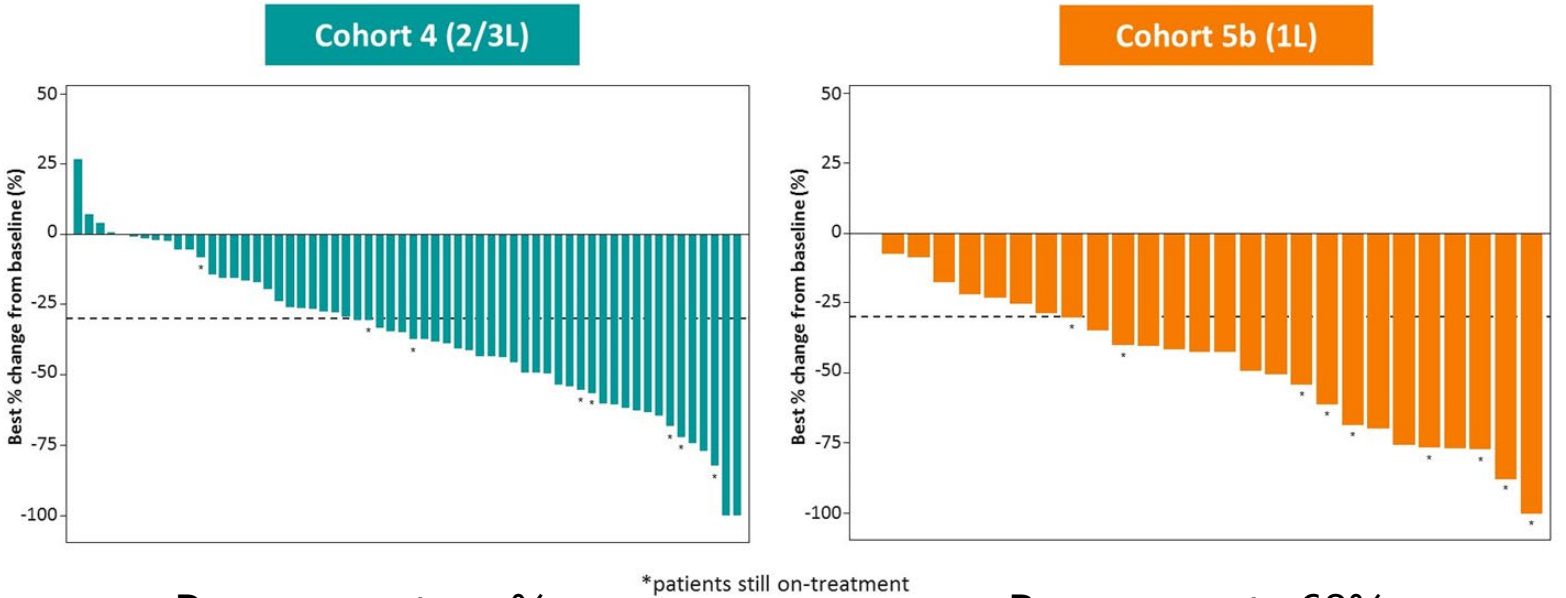
Study methodology:

- Cohort 4 and 5b are each analyzed separately and have independent statistical hypothesis
- Primary (ORR) and key secondary (DOR) endpoints based on BIRC including 2 parallel independent radiology reviewers (+ additional one for adjudication)
- Efficacy endpoints based on BIRC and investigator assessment per RECIST 1.1

Data cut off: April 15, 2019; median duration of follow-up for DOR: 9.7 months in Cohort 4 and 9.6 months in Cohort 5b
Additional data on *MET* mutated patients will be generated in Cohort 6 (2L; N~30) and Cohort 7 (1L; N~27)

Wolf et al, ASCO 2019
ASCO 2020

Capmatinib in MET exon 14 NSCLC



Response rate 41%
(95% CI 29-53)

Response rate 68%
(95% CI 48-84)

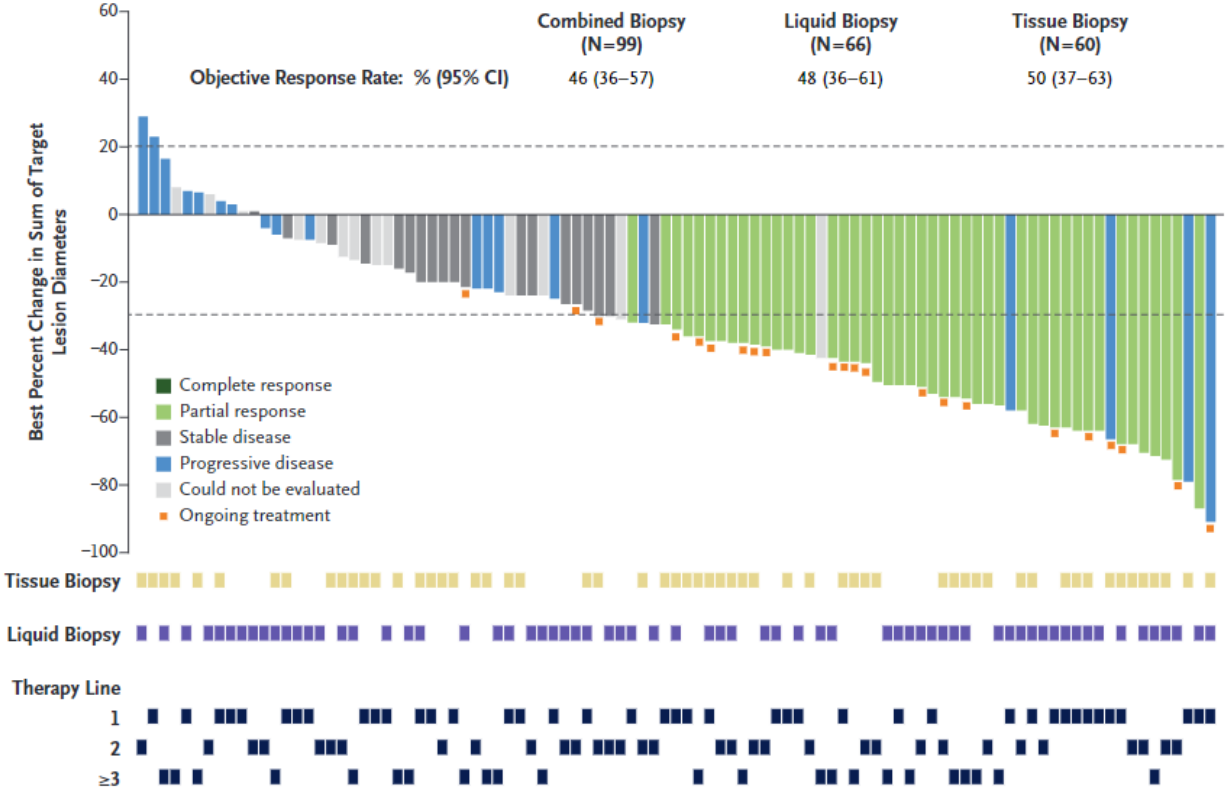
Wolf et al, ASCO 2019, Capmatinib prescribing information, accessed May 2020

FDA grants accelerated approval to capmatinib for metastatic non-small cell lung cancer

Drug Approvals and Databases

On May 6, 2020, the Food and Drug Administration granted accelerated approval to

Tepotinib in Patients with MET exon 14 NSCLC



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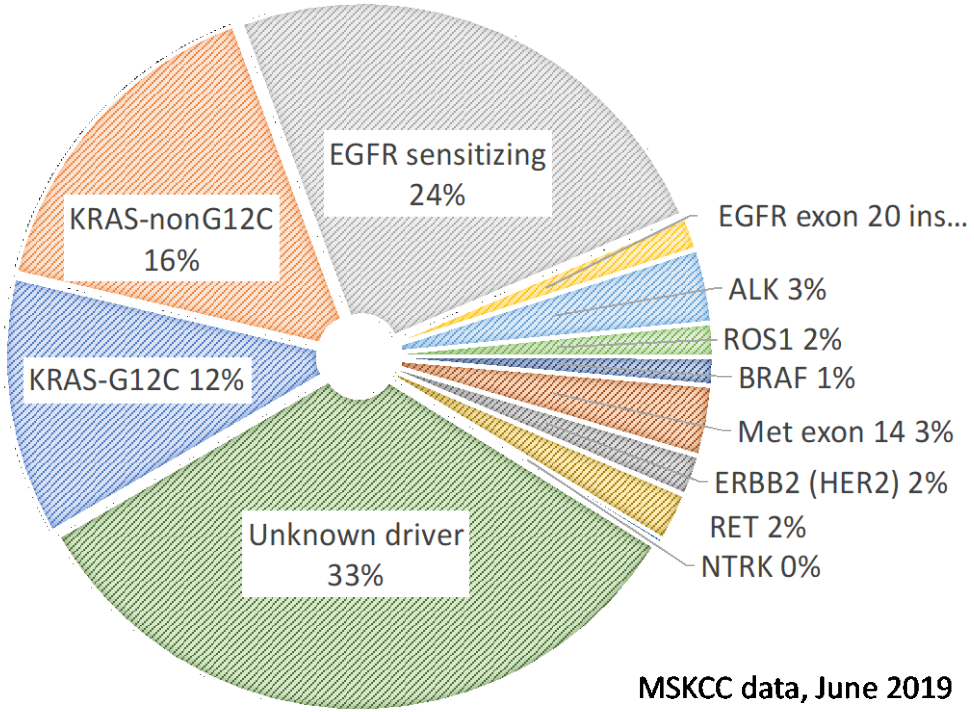
Paik et al, ASCO 2020/NEJM 2020

Molecular Subtypes of Lung Cancer

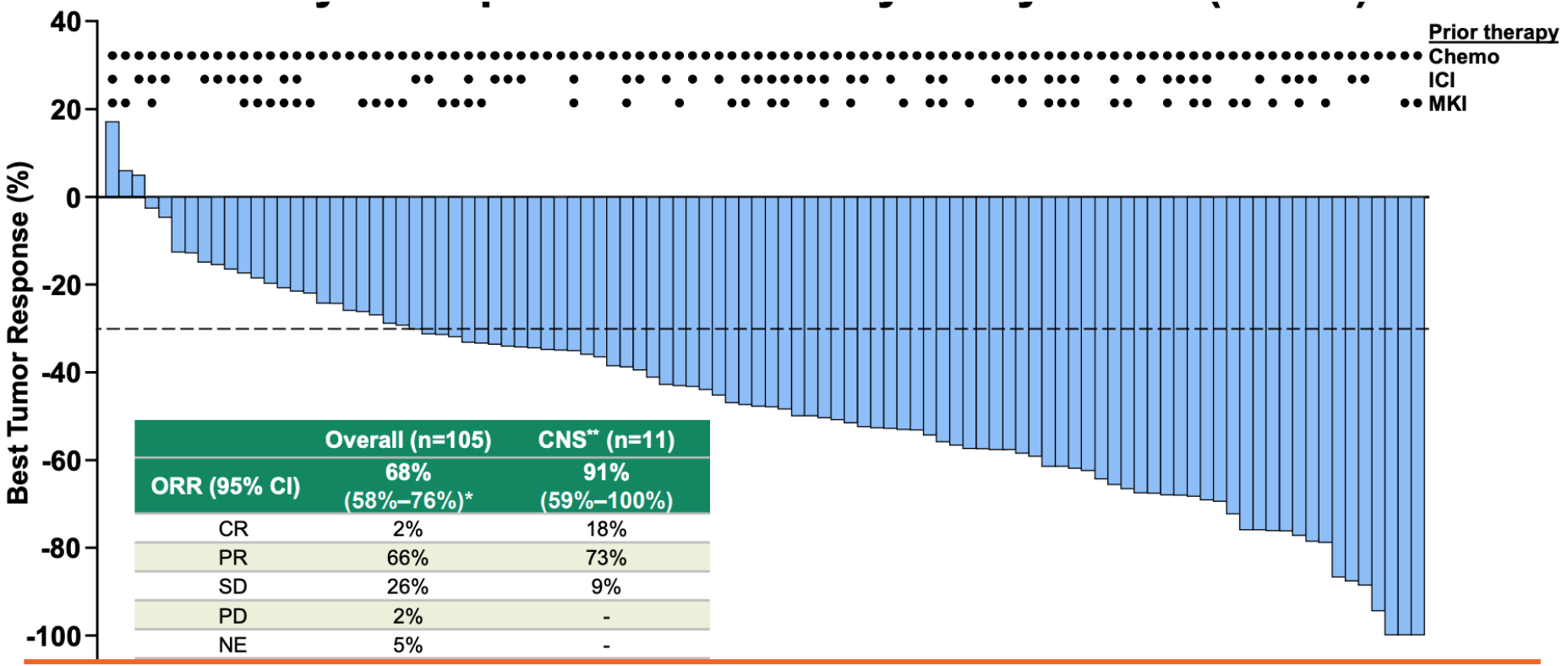


MSKCC data, June 2019

Key Subtypes

EGFR
ALK
ROS1
BRAF
NTRK
MET exon 14
RET

Selpercatinib in patients with RET positive NSCLC

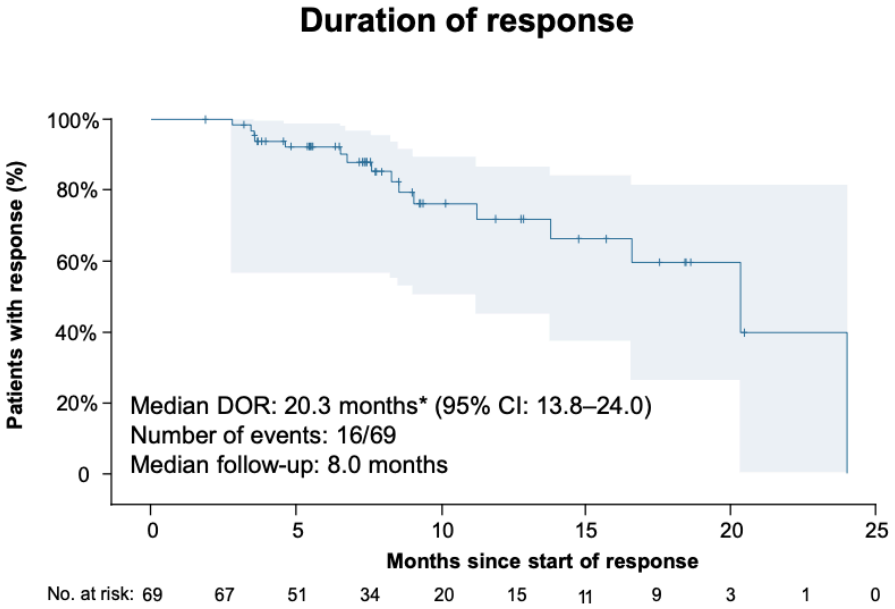


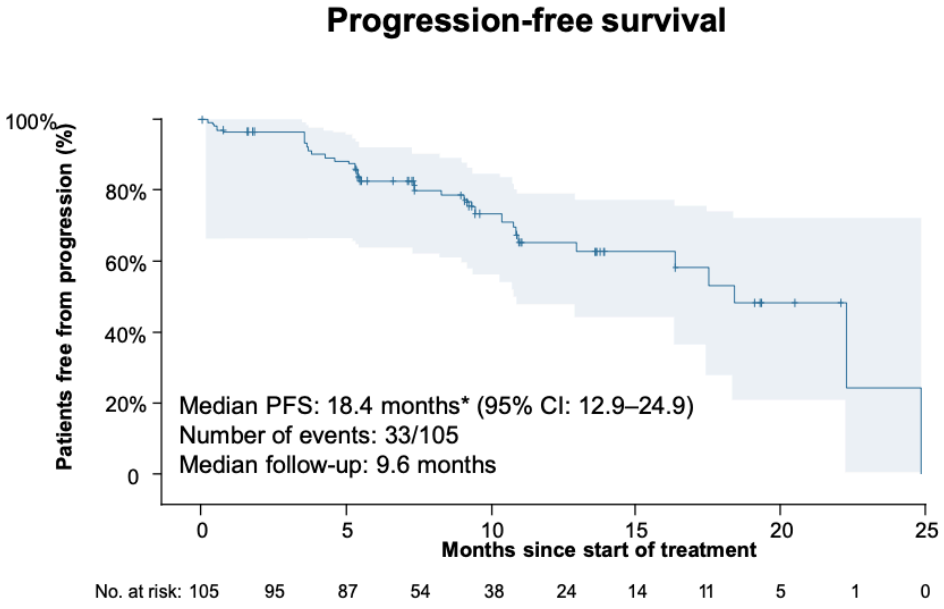
	Overall (n=105)	CNS** (n=11)
ORR (95% CI)	68% (58%–76%)*	91% (59%–100%)
CR	2%	18%
PR	66%	73%
SD	26%	9%
PD	2%	-
NE	5%	-

Memorial Sloan Kettering Cancer Center

Drilon et al, WCLC 2019

Selpercatinib in patients with RET positive NSCLC





Drilon et al, WCLC 2019

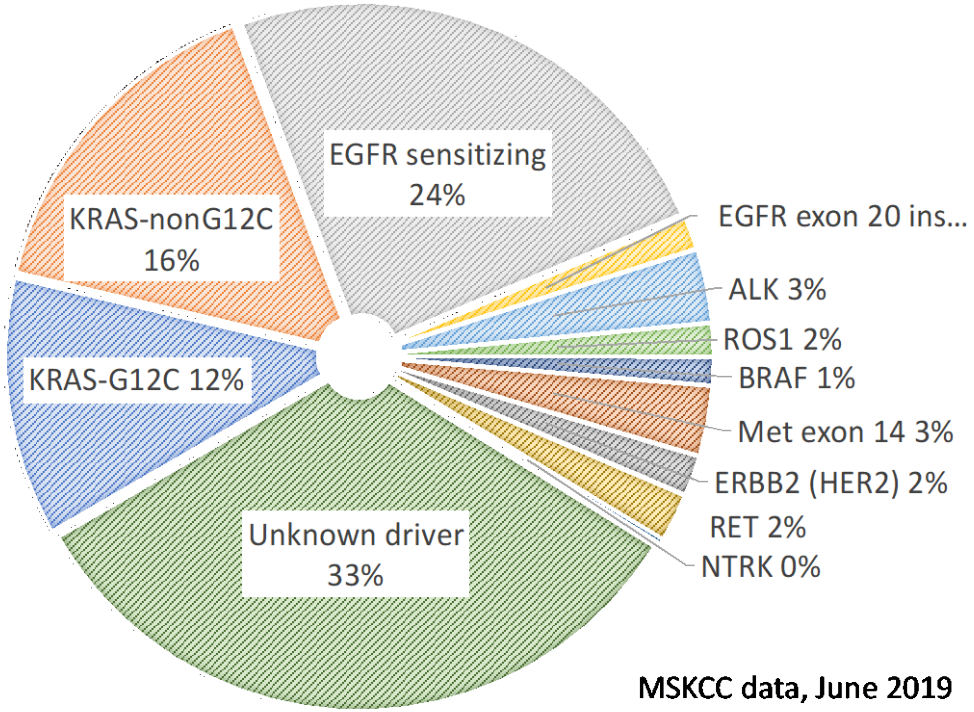
Targeted Therapies in Metastatic NSCLC

- There are now targeted therapies available for:
  - EGFR
  - ALK
  - ROS1
  - BRAF
  - RET
  - MET exon 14
  - RET
  - NTRK

  You need to test for these or you won't find them!

Newly approved drugs:
- Capmatinib for MET exon 14
- Selpercatinib for RET

There are Molecular Subtypes of Lung Cancer

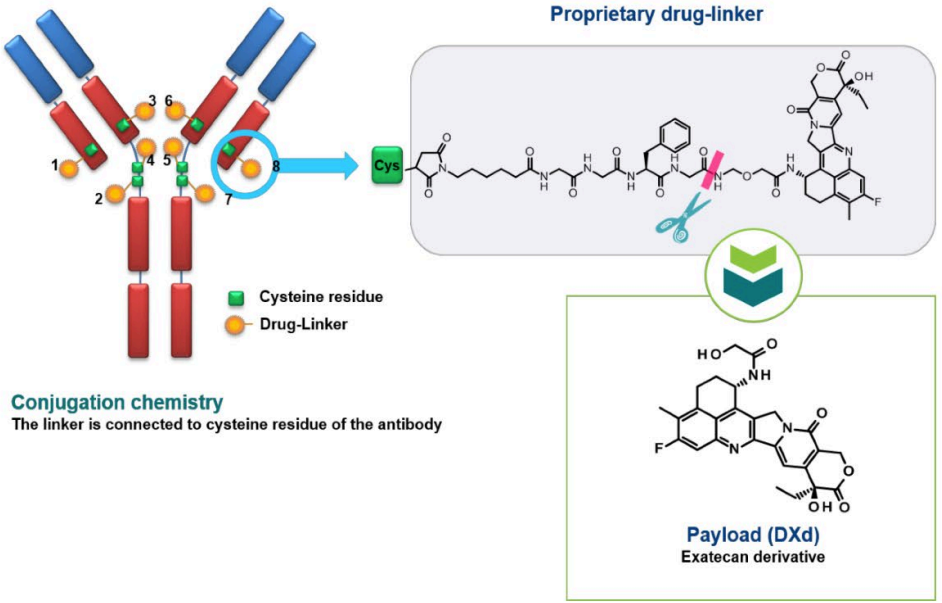


MSKCC data, June 2019

Key Subtypes

EGFR
ALK
ROS1
BRAF
RET
MET Exon14
NTRK

Trastuzumab Deruxtecan



- *Payload with a different mechanism of action*
- *High potency of payload*
- *Payload with short systemic half-life*
- *Bystander effect*
- *Stable linker-payload*
- *Tumor-selective cleavable linker*
- *High drug-to-antibody ratio (7–8)*

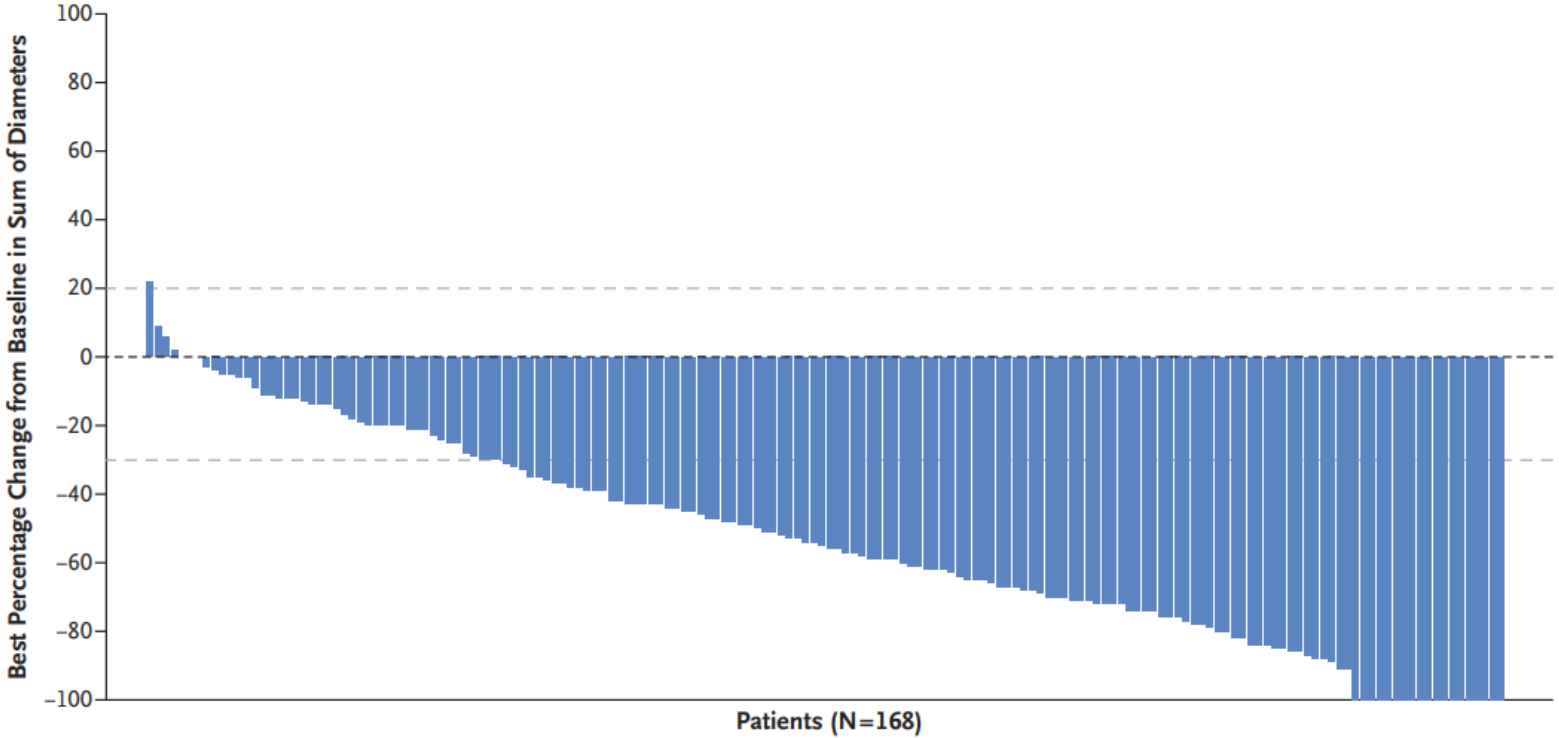
Tsurutani et al, WCLC 2018

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer

S. Modi, C. Saura, T. Yamashita, Y.H. Park, S.-B. Kim, K. Tamura, F. Andre, H. Iwata, Y. Ito, J. Tsurutani, J. Sohn, N. Denduluri, C. Perrin, K. Aogi, E. Tokunaga, S.-A. Im, K.S. Lee, S.A. Hurvitz, J. Cortes, C. Lee, S. Chen, L. Zhang, J. Shahidi, A. Yver, and I. Krop, for the DESTINY-Breast01 Investigators*

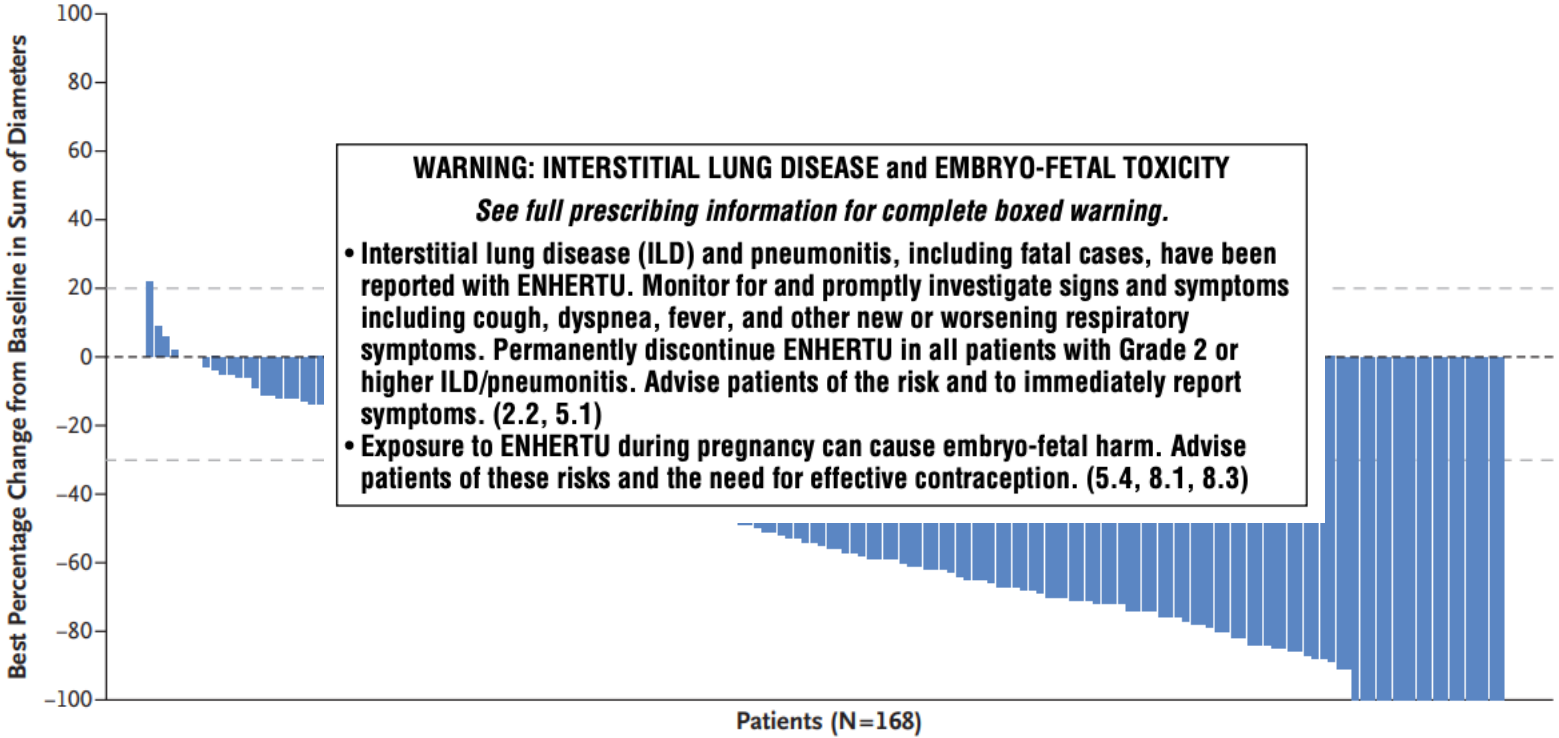
Trastuzumab Deruxtecan in Previously Treated Her2 *amplified* Breast Cancer



Memorial Sloan Kettering Cancer Center

Modi et al NEJM 2020

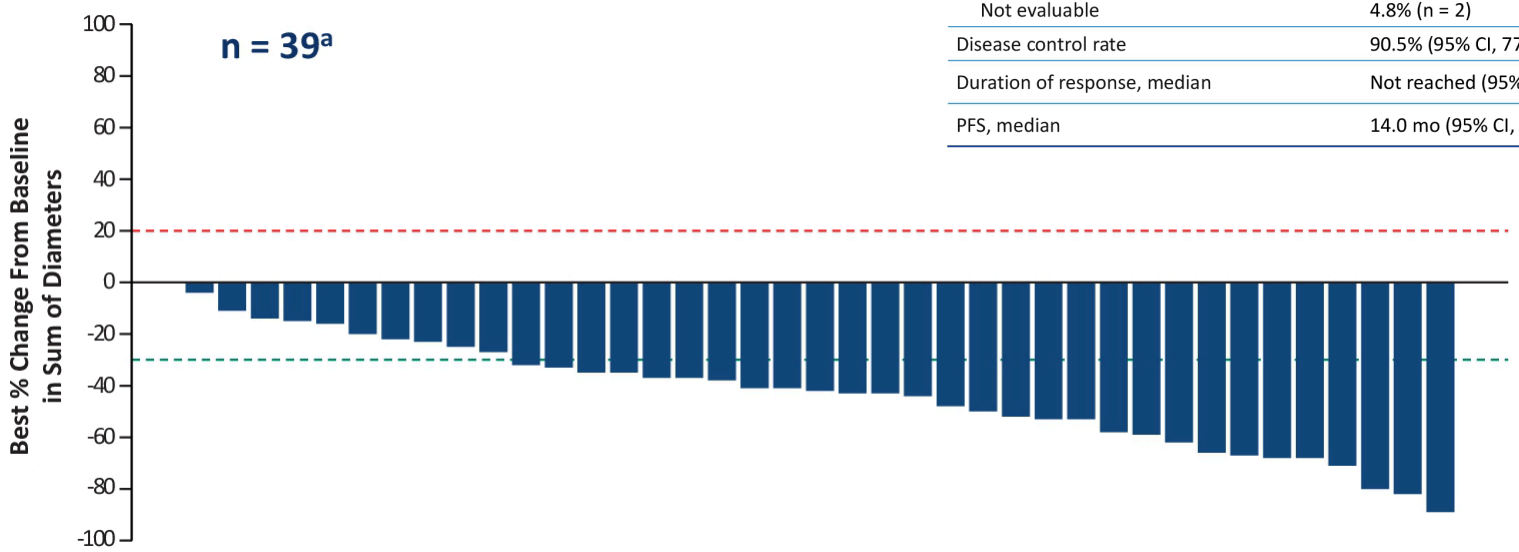
Trastuzumab Deruxtecan in Previously Treated Her2 *amplified* Breast Cancer



Modi et al NEJM 2020

Trastuzumab Deruxtecan in Patients with Her2 Mutated NSCLC

	Patients (N = 42)
Confirmed ORR by ICR	**61.9% (n = 26)** (95% CI, 45.6%-76.4%)
CR	2.4% (n = 1)
PR	59.5% (n = 25)
SD	28.6% (n = 12)
PD	4.8% (n = 2)
Not evaluable	4.8% (n = 2)
Disease control rate	90.5% (95% CI, 77.4%-97.3%)
Duration of response, median	Not reached (95% CI, 5.3 months-NE)
PFS, median	14.0 mo (95% CI, 6.4-14.0 months)



Memorial Sloan Kettering Cancer Center

Smit et al, ASCO 2020

Trastuzumab Deruxtecan in Patients with Her2 Mutated NSCLC

AEs of Special Interest: Interstitial Lung Disease (ILD)

	All Patients (N = 42)					
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	0[a]	5 (11.9)	0	0	0	5 (11.9)

- Median time to onset of investigator-reported ILD was at 86 days (range, 41-255 days)
- 4 patients had drug withdrawn and 1 had drug interrupted
- All patients received steroid treatment
- 2 patients recovered, 1 recovered with sequelae, 1 was recovering, and 1 had not recovered by data-cutoff
- No grade 5 ILD was observed in this cohort

Drug-related; ILD was determined by an Independent ILD Adjudication Committee based on 44 preferred terms.
[a] 1 case of potential grade 1 ILD was pending adjudication.

Targeted Therapies in Metastatic NSCLC

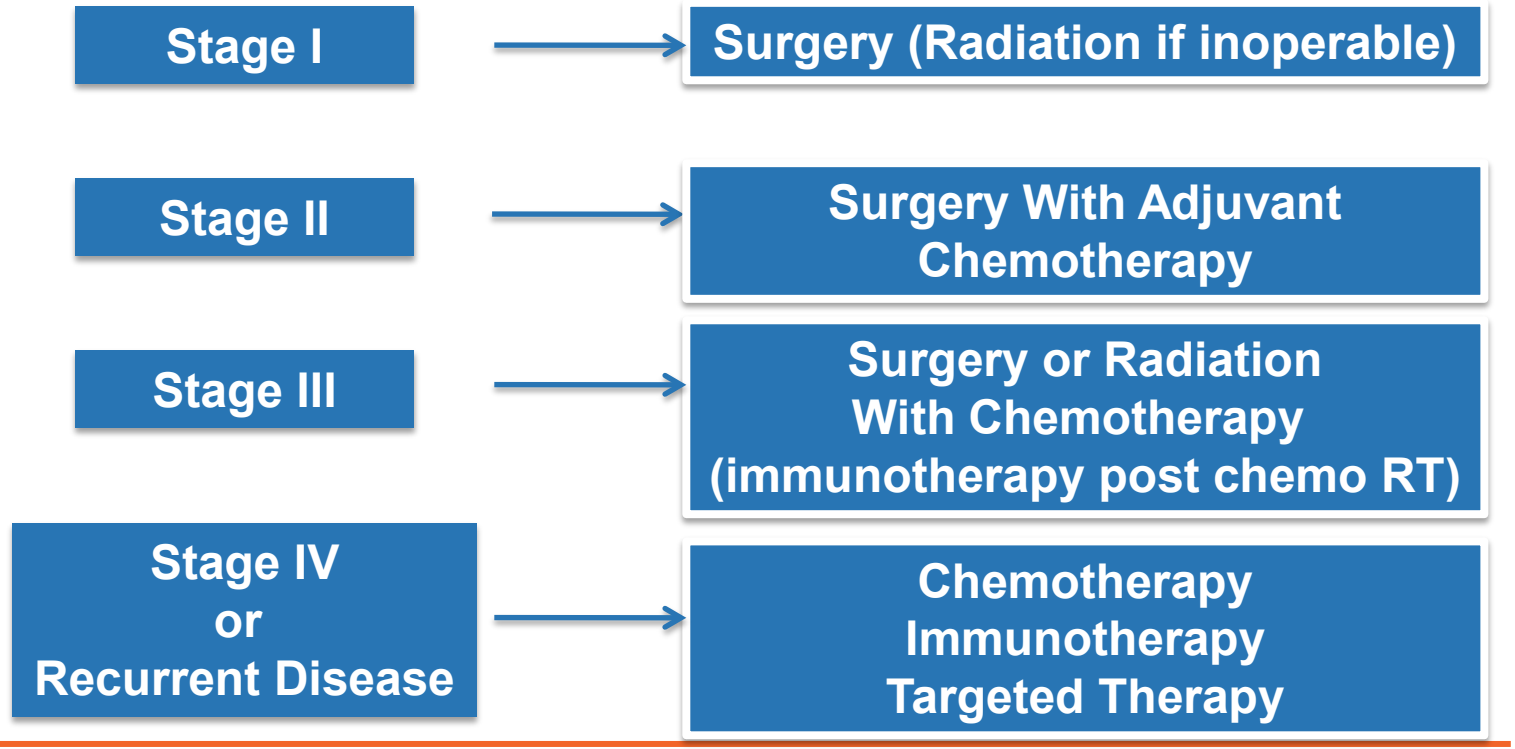
- There are now targeted therapies available for:
  - EGFR
  - ALK
  - ROS1
  - BRAF
  - RET
  - MET exon 14
  - RET
  - NTRK

  You need to test for these or you won't find them!

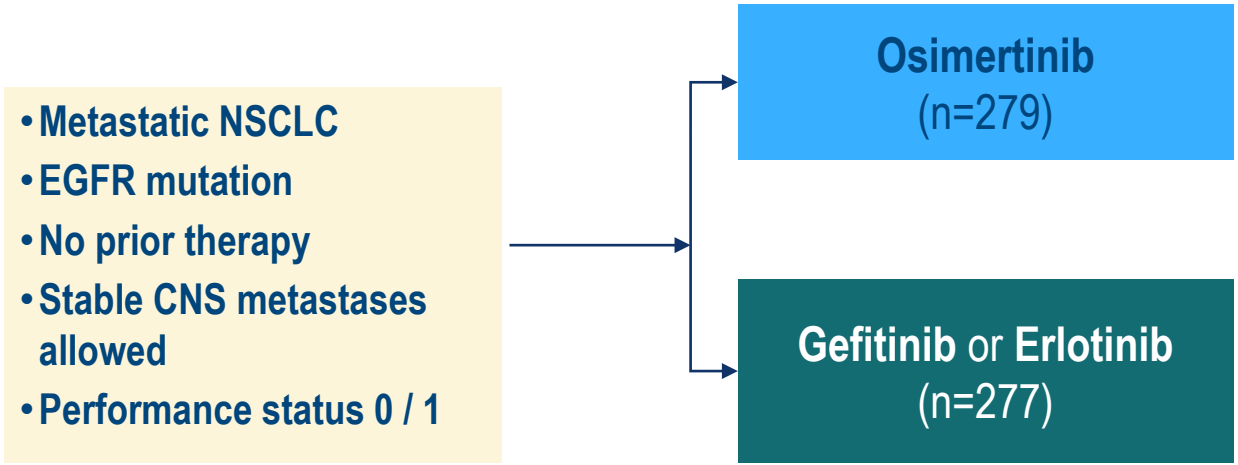
Newly approved drugs:
- Capmatinib for MET exon 14
- Selpercatinib for RET

Perhaps Her2 mutations will be added

General Overview of NSCLC Treatment



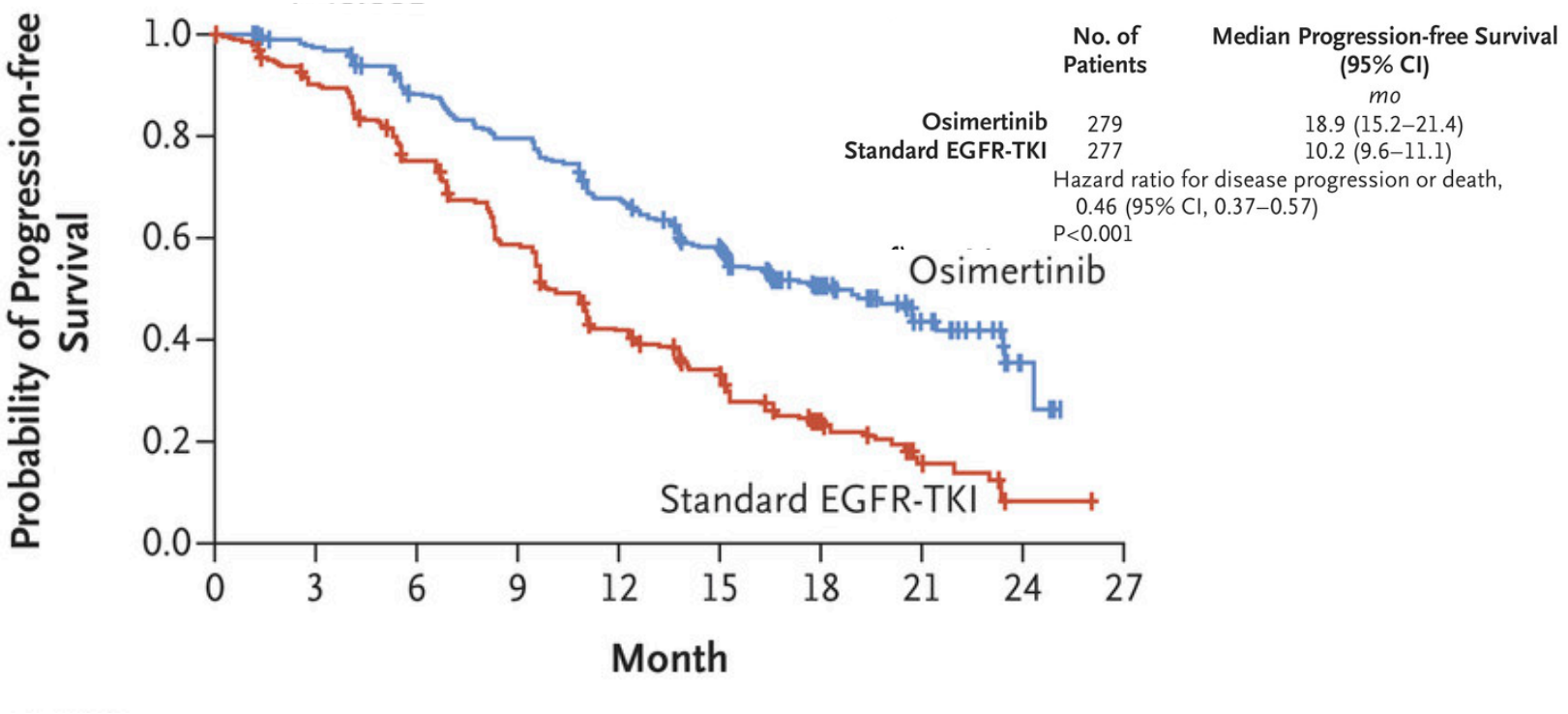
Osimertinib vs Gefitinib/Erlotinib Randomized Trial



- **Primary endpoint:** PFS
- **Secondary endpoints:** response rate, duration of response, disease control rate, depth of response, overall survival, patient reported outcomes, safety

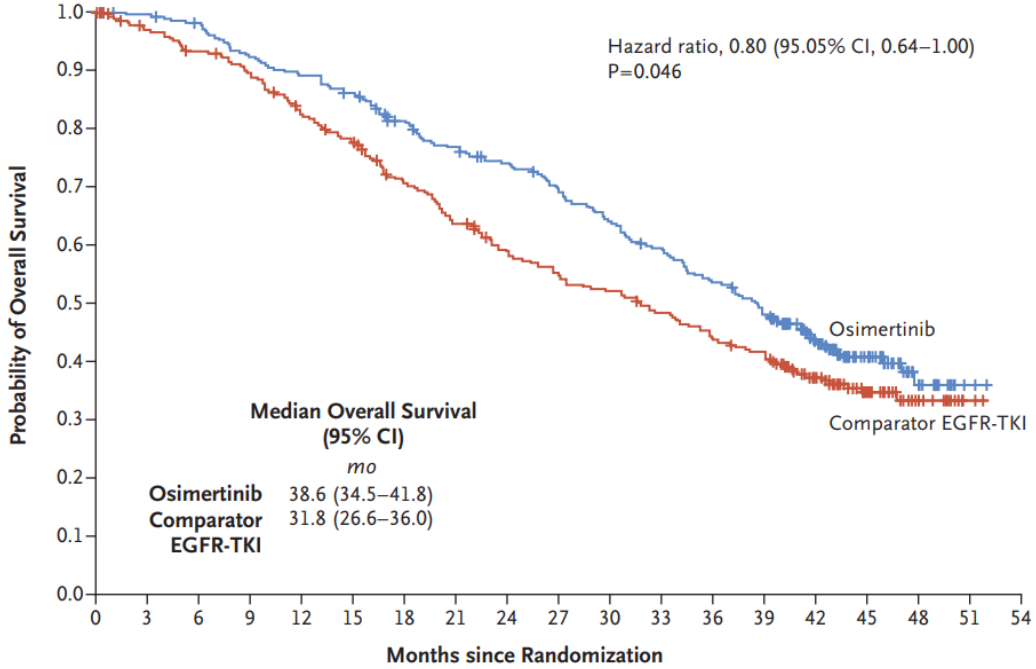
Soria et al, NEJM 2017

Osimertinib vs Gefitinib/Erlotinib as first treatment for NSCLC Progression-Free Survival



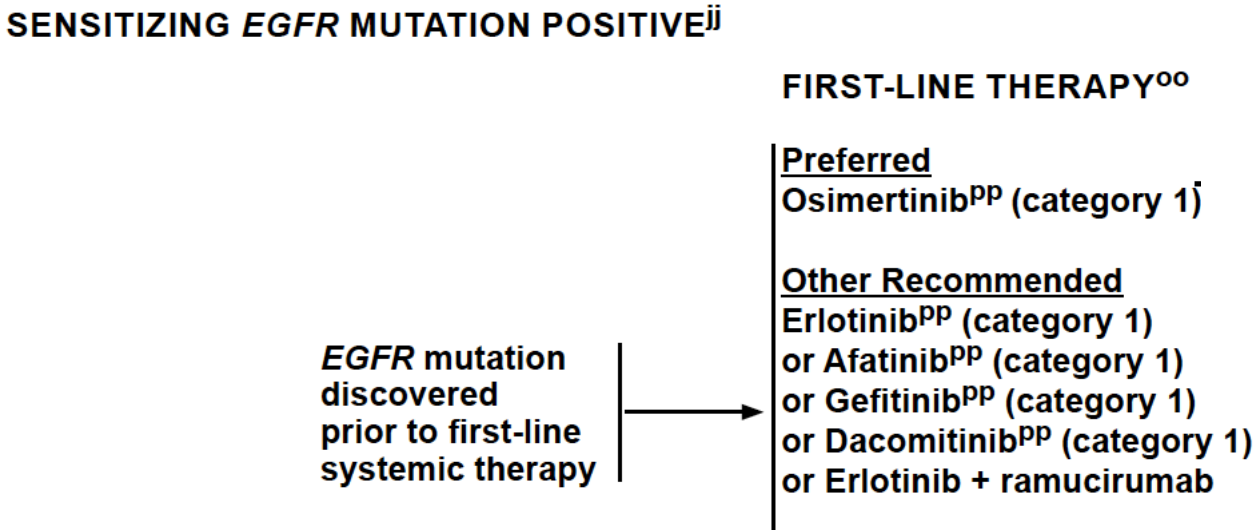
Soria et al, NEJM 2017

Osimertinib vs Gefitinib/Erlotinib as first treatment for NSCLC - Overall Survival



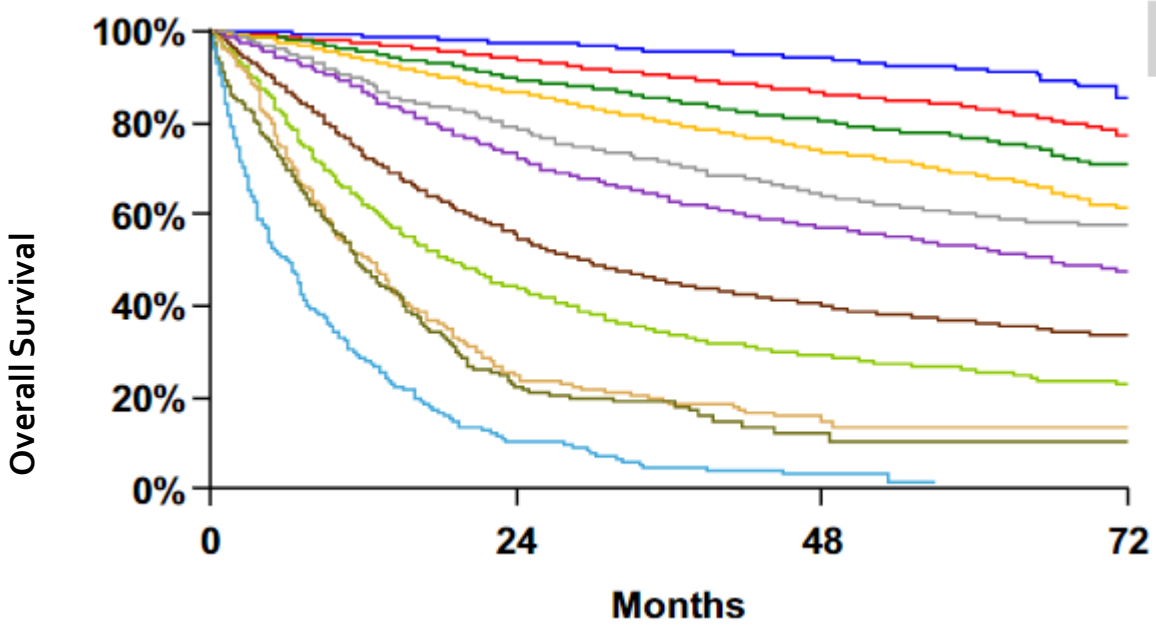
Ramalingam et al, NEJM 2019

1st line Treatment for Patients with EGFR mutant NSCLC



Outcomes by pathologic stage for NSCLC (v8)

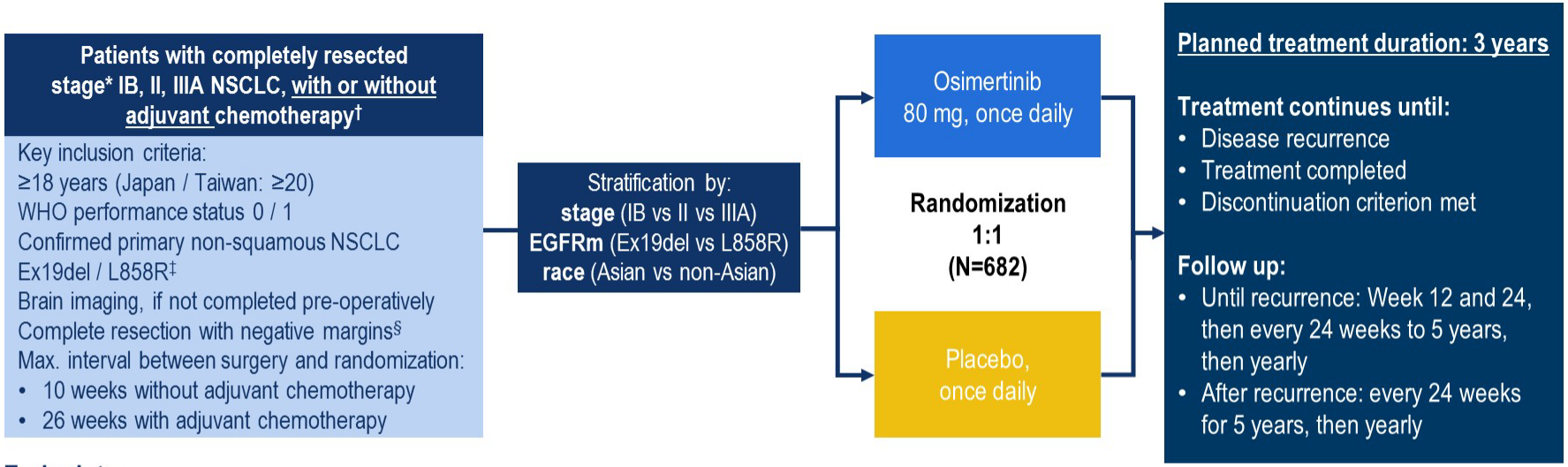
Surgically resected patients, 1999 – 2010



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

Goldstraw, et al. *J Thorac Oncol*. 2015

Osimertinib vs placebo after surgery for Stage I-III NSCLC



Endpoints

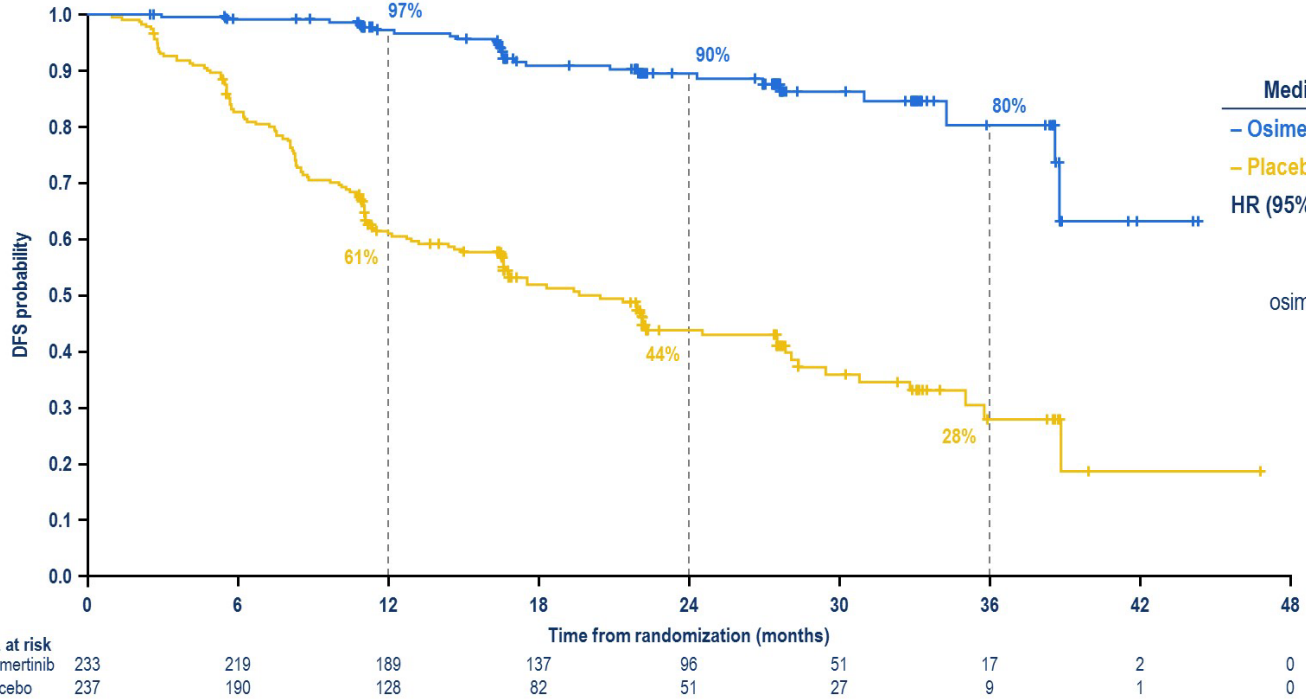
- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

Herbst et al, ASCO 2020

Osimertinib vs placebo after surgery for Stage I-III NSCLC

Primary endpoint: DFS in patients with stage II/IIIA disease



Median DFS, months (95% CI)	
– Osimertinib	NR (38.8, NC)
– Placebo	20.4 (16.6, 24.5)
HR (95% CI)	0.17 (0.12, 0.23); p<0.0001

Maturity 33%:
osimertinib 11%, placebo 55%

Herbst et al, ASCO 2020

Osimertinib vs placebo after surgery for Stage I-III NSCLC

DFS by stage

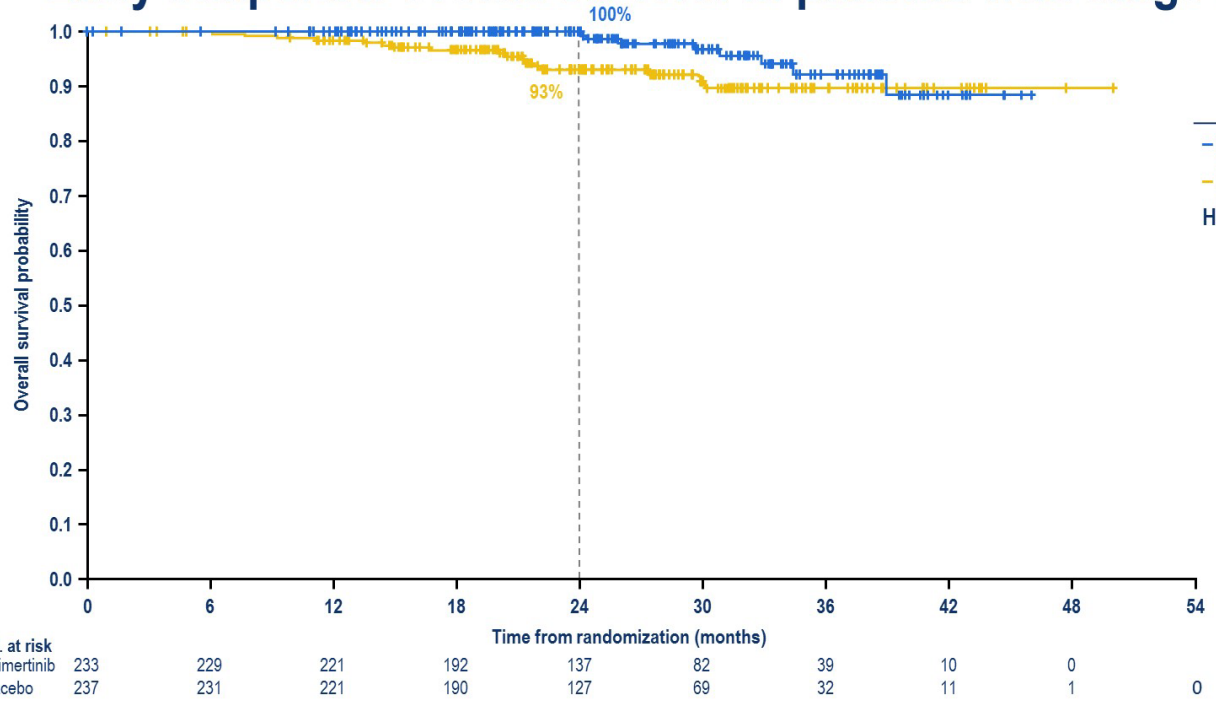
	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	**0.50 (0.25, 0.96)**	**0.17 (0.08, 0.31)**	**0.12 (0.07, 0.20)**

- In the osimertinib arm, 2 year DFS rates were consistent across stages IB, II, and IIIA disease
- Maturity (overall population: stage IB / II / IIIA) 29%: osimertinib events 12%, placebo events 46%

Herbst et al, ASCO 2020

Osimertinib vs placebo after surgery for Stage I-III NSCLC

Early snapshot: overall survival in patients with stage II/IIIA disease



Median OS, months (95% CI)	
– Osimertinib	NR (NC, NC)
– Placebo	NR (NC, NC)
HR (95% CI)	0.40 (0.18, 0.90)

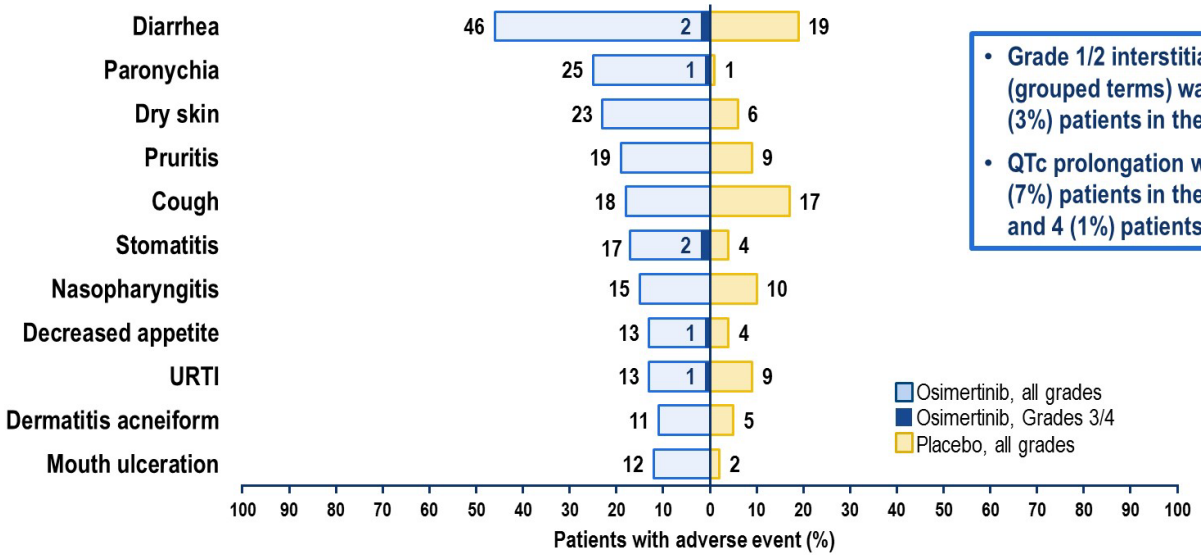
Maturity 5%:
osimertinib 3%, placebo 7%

Herbst et al, ASCO 2020

Osimertinib vs placebo after surgery for Stage I-III NSCLC

All causality adverse events (≥10% of patients)

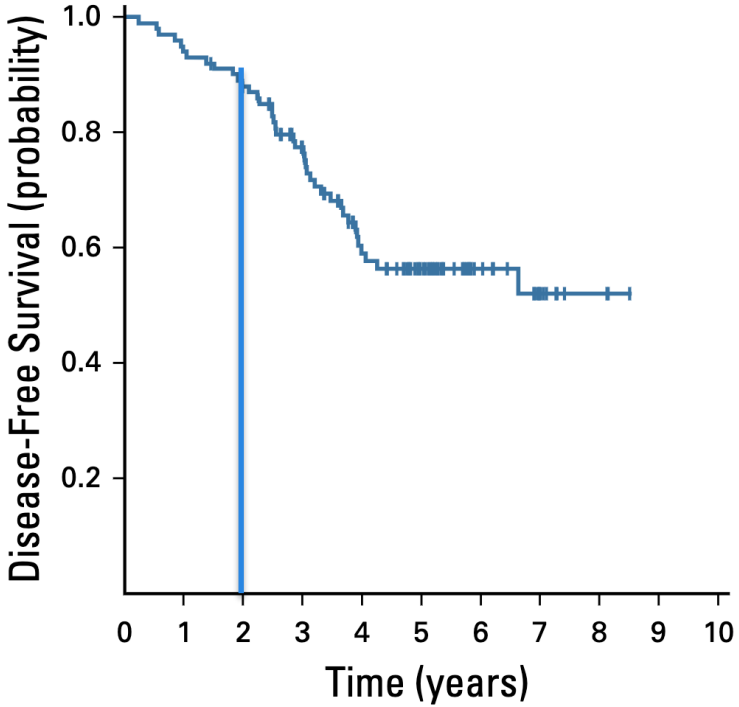
Median duration of exposure: osimertinib: 22.3 months (range 0 to 43), placebo: 18.4 months (range 0 to 48)



- Grade 1/2 interstitial lung disease (grouped terms) was reported in 10 (3%) patients in the osimertinib arm*
- QTc prolongation was reported in 22 (7%) patients in the osimertinib arm and 4 (1%) patients in the placebo arm†

Herbst et al, ASCO 2020

Erlotinib as Adjuvant Therapy (2 years)



Pennell et al, JCO 2018

Questions about adjuvant (post-operative) osimertinib?

- Which is the best population to received?
- Does it cure people or delay progression?
- Does that matter?
- Will it improve overall survival?

Conclusions

- Immune Checkpoint Inhibitor + platinum/etoposide remain the standard of care for patients with extensive stage small cell lung cancer
- A short course chemotherapy with ipilimumab/nivolumab is another option for patients with stage IV NSCLC without an oncogenic driver
- MET exon 14 is a targetable oncogenic driver with treatment options
- HER2 mutations as a targetable oncogenic driver with available treatment options
- We can now consider EGFR targeted therapy in the adjuvant setting

11%

Annals of Oncology
Available online 17 June 2020
In Press, Journal Pre-proof

Original Article

COVID-19 in patients with lung cancer

Jia Luo [1, #], Hira Rizvi [2, #], Isabel R. Preeshagul [1], Jacklynn V. Egger [2], David Hoyos [3], Chaitanya Bandlamudi [4], Caroline G. McCarthy [2], Christina J. Falcon [2], Adam J. Schoenfeld [1, 5], Kathryn C. Arbour [1, 5], Jamie E. Chaft [1, 5], Robert M. Daly [1, 5], Alexander Drilon [1, 5], Juliana Eng [1], Afsheen Iqbal [1], W. Victoria Lai [1, 5], Bob T. Li [1, 5], Piro Lito [1, 5] ... Matthew D. Hellmann [1, 5, 7]

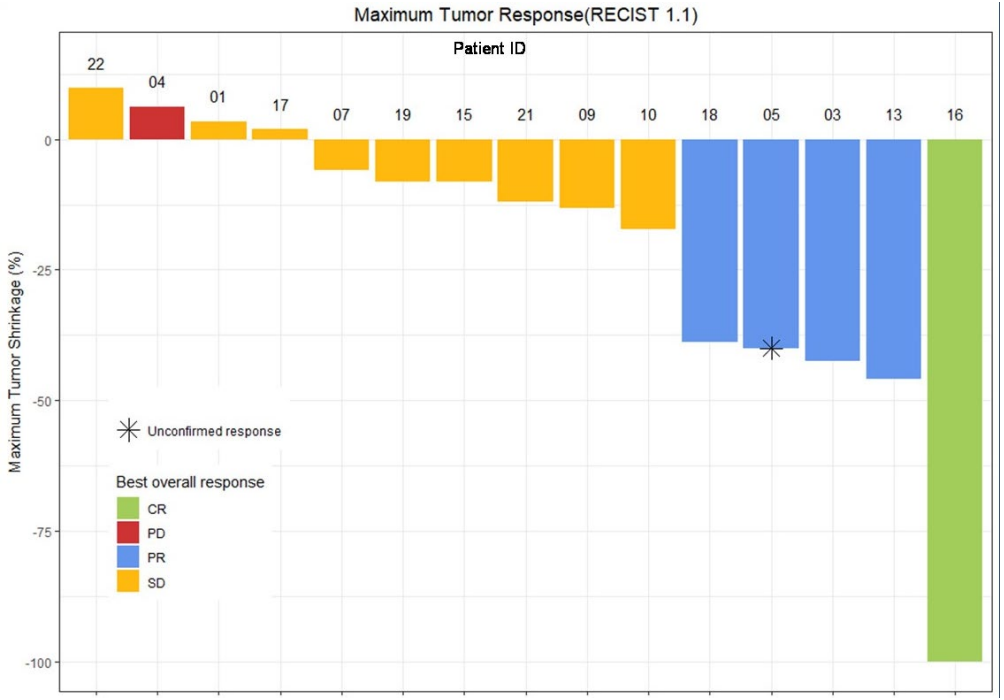
11%

During the peak of COVID-19 in NYC,
among our patients with lung cancer,
just 11% of the deaths were due to COVID-19.
Vast majority died of complications of lung cancer

Osimertinib in EGFR exon 20 insertion NSCLC

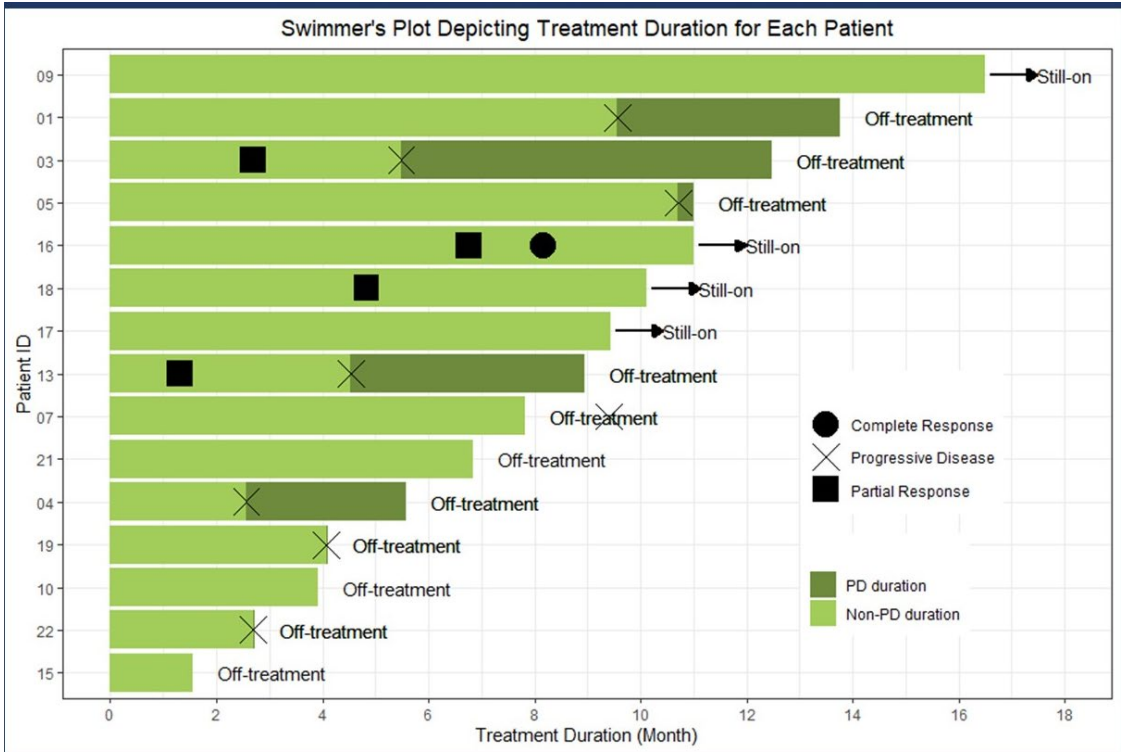
OVERALL EFFICACY:

- **Confirmed ORR:** 4/17, 24%
- **DCR:** 14/17, 82%
- **mPFS:** 9.6 mo (95% CI, 4.1, 10.7)
- **mDOR:** NA (95% CI, 4.7, NA)



Piotrowska et al, ASCO 2020

Osimertinib in EGFR exon 20 insertion NSCLC



Piotrowska et al, ASCO 2020