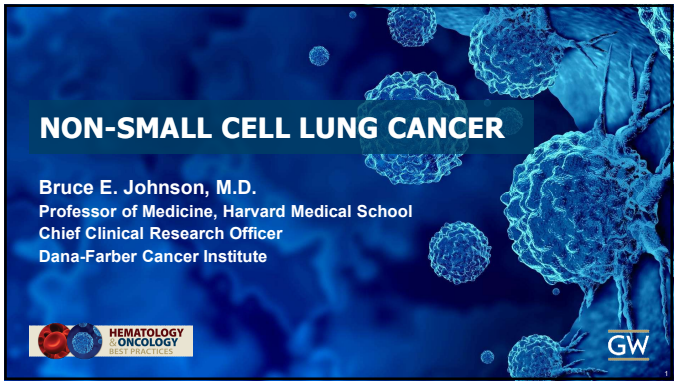


Disclosures

- Financial Relationships with Relevant Commercial Interests
  - Post Marketing Royalties for *EGFR* mutation testing from DFCI
  - Paid Consultant to Novartis, Checkpoint Therapeutics, Daichi Sankyo, GSK, Hengrui Therapeutics, Boston Pharmaceuticals, Genentech
  - 1-Day Advisory Boards: Chugai, Foundation Medicine, Lilly, G1 Therapeutics, Jazz Pharmaceuticals, Janssen Scientific Affairs
  - Unpaid Member of Steering Committee for Pfizer
  - Research Support from Novartis, Cannon Medical Imaging
- Resolution
  - Reviewed and found to be unbiased

GW 2

Management of Untreated & Treated NSCLC

- **Screening for Lung Cancer**
- Adjuvant Therapy for Early Stage
- Chemotherapy With Surgery and Radiation in Locally Advanced Disease
- Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)
- Relapsed Non-Small Cell Lung Cancer

GW 3

Screening: NLST and Dutch-Belgian Trials

NLST

- Aug 2002-Sep 2004
- 53,454 participants at risk for lung cancer
- Smoked >1 package of cigarettes per day for 30 years
- Quit <15 Years Ago
- Age 55-74

Aberle, et al. *NEJM*. 365:395, 2011
NLungST Research Team. *NEJM*. 368:1980, 2013

NELSON

- Dec 2003-Jun 2006
- 15,792 participants at risk for lung cancer
- Smoked >10 cigarettes per day for 30 years, >15 cigarettes per day for 25 years
- Age 55-74

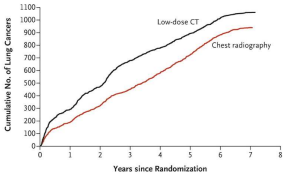
de Koning, et al. *N Engl J Med*. 2020 382:503

Primary Endpoints: Mortality Due to Lung Cancer

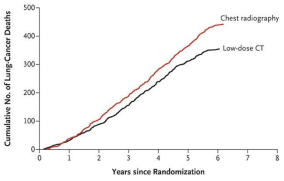
4

Screening for Lung Cancer: NLST

Lung Cancer



Death from Lung Cancer

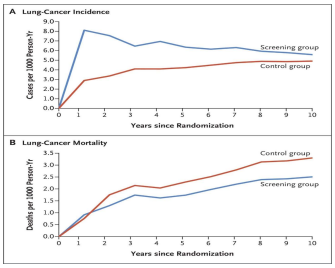


Aberle, et al. *NEJM*. 365:395, 2011; National Lung Screening Trial Research Team *NEJM*. 368:1980, 2013

5

Screening for Lung Cancer: NELSON

Mortality Rate Ratio



de Koning, et al. *N Engl J Med*. 2020 382:503

6

Screening Recommendations

American College of Chest Physicians, ASCO, US Preventive Services Task Force

- Both Screening Trials showed a Reduction in Lung Cancer Mortality in the Screened Populations of Approximately 20%
- U.S. Preventive Services Task Force recommends annual LC screening with low-dose computed tomography in adults ages 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.
- Centers for Medicare & Medicaid Services (CMS) determined that the evidence is sufficient to add a LC screening counseling and shared decision-making visit, and for appropriate beneficiaries, annual LC screening for with low dose computed tomography (LDCT) as an additional preventive service benefit under Medicare program (Feb 15, 2015)

https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening

7

Management of Untreated & Treated NSCLC

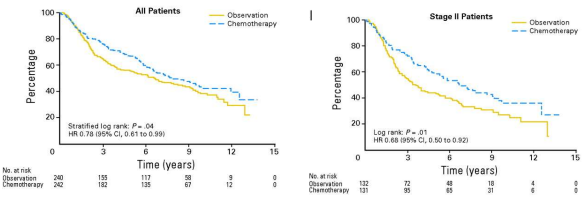
- Screening for Lung Cancer
- **Adjuvant Therapy for Early Stage**
- Chemotherapy With Surgery and Radiation in Locally Advanced Disease
- Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)
- Relapsed Non-Small Cell Lung Cancer

8

Adjuvant Therapy for Early Stage NSCLC

JBR.10: Adjuvant Cisplatin/Vinorelbine

Cisplatin/Vinorelbine vs Placebo in Stages IB-II NSCLC



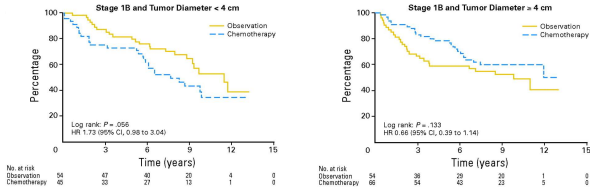
Butts CA, et al. *J Clin Oncol.* 2010;28(1):29-34

9

Adjuvant Therapy for Early Stage NSCLC

JBR.10: Adjuvant Cisplatin/Vinorelbine

Impact of Adjuvant Chemotherapy in Tumors ≥4 cm



Butts CA, et al. *J Clin Oncol.* 2010;28(1):29-34

Adjuvant Therapy for Early Stage NSCLC

Benefits of Adjuvant Chemotherapy for Surgically Resected NSCLC

	# Pts	↑ 5 yr (%)	HR	95% CI	*P*
	1209	3	0.96	0.81-1.13	.59
	1867	4	0.86	0.76-0.98	.03
	482	15	0.70	0.52-0.92	.01
	344	2	0.80	0.60-1.07	.10
	840	8	0.79	0.66-0.95	.01
Meta06	4584	4	0.89	0.82-0.96	.005

JNCI 03; NEJM 04; *NEJM* 05; *J Clin Oncol* 08; *Lancet Oncol* 06

Adjuvant Therapy for Early Stage NSCLC

Osimertinib vs. Placebo for EGFR Mutant NSCLC

Patients with Stages IB, II, and III Resec NSCLC

Key inclusion criteria
- ≥18 years*
- WHO performance status 0 / 1
- Exon 19 deletion / L858R
- Complete Resection
- No prior systemic therapy

Osimertinib (80 mg p.o. qd) (n=279)

Randomized 1:1
682 from 2015 to 2019

Placebo

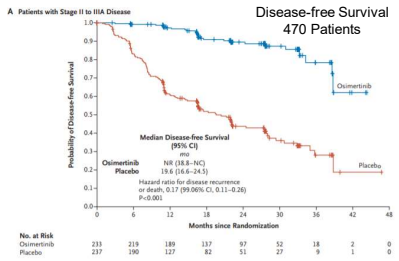
3 Years of Treatment Rx Continues to Completion, Recurrence, or Discontinuation

- **Primary endpoint:** Disease-Free Survival for Stages II and III
- **Secondary endpoints:** Disease-Free Survival in the Overall Population
- April 2020: Data Safety Monitoring Committee recommends trial be unblinded at a trial level early to complete primary reporting

Wu, et al. *N Engl J Med.* 2020 epub Sep 19.

Adjuvant Therapy for Early Stage NSCLC

Osimertinib vs. Placebo for EGFR Mutant NSCLC



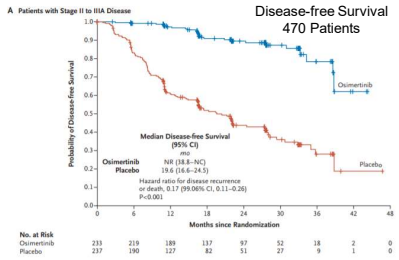
FDA APPROVED 2021 Osimertinib

Wu, et al. *N Engl J Med.* 2020 epub Sep 19.

GW 13

Adjuvant Therapy for Early Stage NSCLC

Osimertinib vs. Placebo for EGFR Mutant NSCLC



FDA APPROVED 2021 Osimertinib

Wu, et al. *N Engl J Med.* 2020 epub Sep 19.

GW 14

Adjuvant Therapy for Early Stage

2021 ASCO ANNUAL MEETING

IMpower010: Study Design

Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7
- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine
1-4 cycles
N=1280

R 1:1

No crossover

Atezolizumab 1200 mg q21d 16 cycles
N=1005

BSC

Survival follow-up

Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a] Per SP142 assay.

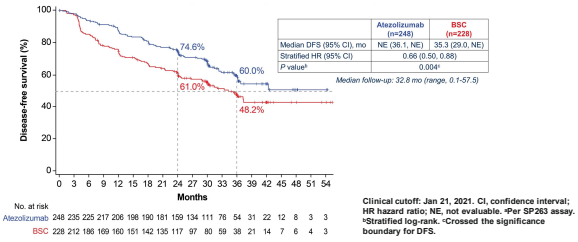
Wakelee, Heather. 2021 ASCO Annual Meeting #8500. Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

GW 15

Adjuvant Therapy for Early Stage

2021 ASCO ANNUAL MEETING

IMpower010: DFS in PD-L1 TC≥1T[a] Stage II-IIIA Population (primary endpoint)



	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

Median follow-up: 32.8 mo (range, 0.1-57.5)

Clinical cutoff: Jan 21, 2021. CI, confidence interval; HR hazard ratio; NE, not evaluable. [a]Per SP263 assay. [b]Stratified log-rank. [c]Crossed the significance boundary for DFS.

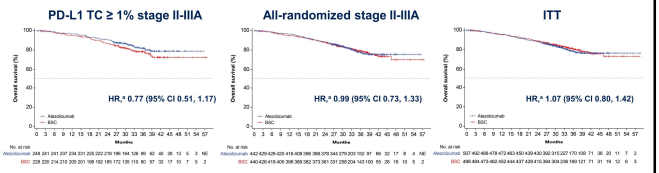
GW

16

Adjuvant Therapy for Early Stage

2021 ASCO ANNUAL MEETING

IMpower010: Early OS Data at Interim DFS Analysis



- OS data were immature at this pre-planned DFS interim analysis
  - OS in the ITT population was not formally tested
  - A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population

Clinical cutoff: Jan 21, 2021. *Stratified

GW

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Adjuvant Therapy for Early Stage NSCLC

Adjuvant Chemo for Surgically Resected NSCLC

- Four cycles adjuvant cisplatin-based therapy is standard of care for resected stage 1B>4cm, II and III NSCLC (ASCO guidelines)
- Osimertinib for L858R and exon 19 deletion *EGFR* mutations after adjuvant chemotherapy
- Adjuvant therapy with atezolizumab in patients with >1% PD-L1 is promising and we await more mature data

GW

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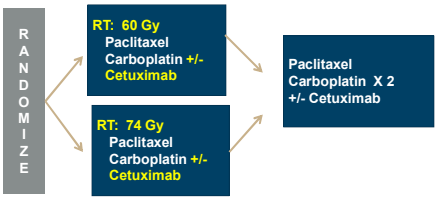
Management of Untreated & Treated NSCLC

- Screening for Lung Cancer
- Adjuvant Therapy for Early Stage
- **Chemotherapy with Surgery & Radiation in Locally Advanced Disease**
- Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)
- Relapsed Non-Small Cell Lung Cancer

Stage III NSCLC

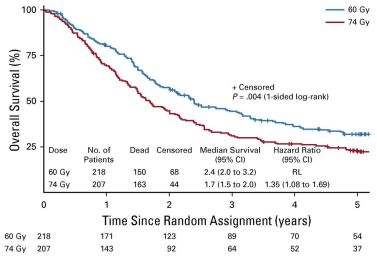
RTOG 0617: Pts with Inoperable Stage III NSCLC



Bradley JD. *Lancet Oncology* 2015; 6: 87

Stage III NSCLC

RTOG 0617 5-Year Follow-up: 60 vs 74 Gy



Bradley JD. *J Clin Oncol* 2020 Mar 1;38(7):706

Stage III NSCLC

Durvalumab vs Observation in Maintenance

Two Cycles of Platinum-Based Chemotherapy (Etoposide, Vinblastine, Vinorelbine, a Taxane, or Pemetrexed) Plus 5400-6600 Gy Chest RT Concurrently

Eligibility
- Nonsquamous NSCLC
  - Stage IIIA/IIIB
  - PS 0,1
  - Radiation plan ≤20 Gy to <35% Lung Vol
  - Randomized up to 6 Weeks after Chest RT

RANDOMIZE*

2 → **Durvalumab 10 mg/kg IV every 2 weeks for 1 Yr**

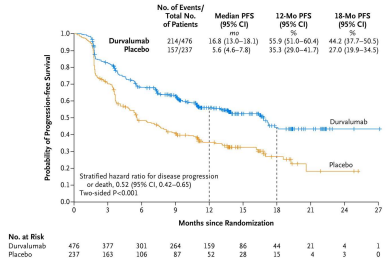
1 → **Observation**

Antonia, et al. *N Engl J Med.* 2017; 377:1919

22

Stage III NSCLC

Durvalumab vs Observation in Maintenance

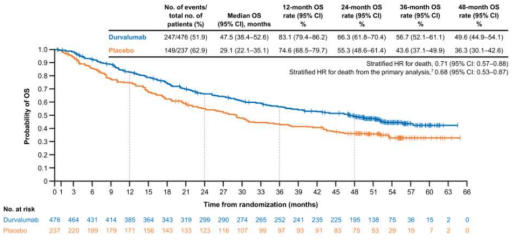


Antonia, et al. *N Engl J Med.* 2017; 377:1919

23

Stage III NSCLC-4 Year Follow-up

Durvalumab vs Observation in Maintenance



FDA APPROVED 2018 Durvalumab

Faivre-Finn et al. *J Thorac Oncol* 2021 May;16(5):860

24

Stage III NSCLC

Management of Patients with N2 Disease

- Patients should be treated with concurrent chest irradiation and platin-based chemotherapy (etoposide or pemetrexed are appropriate). Chest radiotherapy given to 60 Gy is an appropriate dose.
- Durvalumab should be administered to fit patients within two months of when the combined modality is completed
- Pemetrexed cisplatin may be considered in addition to etoposide cisplatin for non-squamous NSCLC
- Paclitaxel/carboplatin is also a reasonable combination

Management of Untreated & Treated NSCLC

- Screening for Lung Cancer
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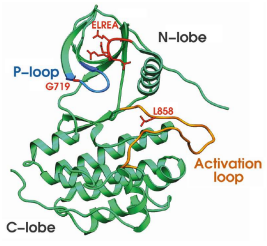
- **Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)**
- Relapsed Non-Small Cell Lung Cancer

Metastatic NSCLC

Epidermal Growth Factor Receptor Mutations



13 of 14 Patients with Response to Gefitinib Had EGFR Mutation

The NEW ENGLAND JOURNAL of MEDICINE
Lynch et al. 2004

Science
Paez et al. 2004

Metastatic NSCLC

EGFR 3rd Gen TKI: Osimertinib vs Gefitinib or Erlotinib

Patients with locally advanced or metastatic NSCLC

Key inclusion criteria
- ≥18 years*
- WHO performance status 0 / 1
- Exon 19 deletion / L858R (enrolment by local‡ or central‡ EGFR testing)
- No prior systemic therapy

Osimertinib (80 mg p.o. qd) (n=279)

Randomized 1:1

EGFR-TKI SoC§: **Gefitinib** (250 mg p.o. qd) or **Erlotinib** (150 mg p.o. qd) (n=277)

RECIST 1.1 assessment every 6 weeks¶ until objective progressive disease

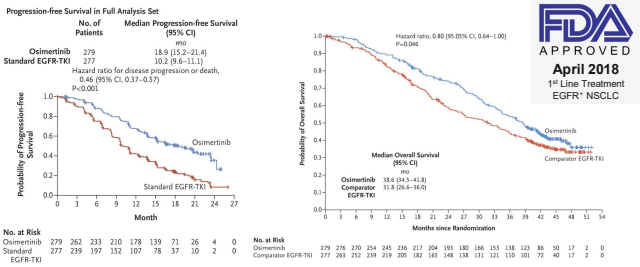
Endpoints
- **Primary endpoint:** PFS based on investigator assessment
- **Secondary endpoints:** objective response rate and survival, patient reported outcomes, safety

Soria, et al. *N Engl J Med.* 2018 Jan 11;378(2):113

28

Metastatic NSCLC

Osimertinib vs EGFR-TKI for Previously Untreated Pts



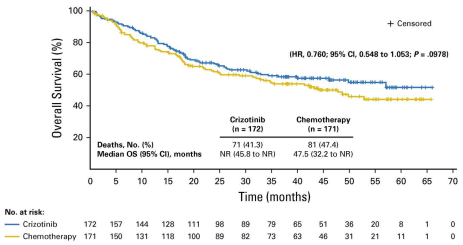
FDA APPROVED
April 2018
1st Line Treatment EGFR+ NSCLC

Ramalingham, et al. *NEJM* 2018; 378:113; Ramalingham, et al. *N Engl J Med.* 2020 Jan 2;382(1):41

29

Metastatic NSCLC

Crizotinib for 1st Line NSCLC: 4 Year Follow-up



Solomon, et al. *J Clin Oncol.* 2018 Aug 1;36(22):2251-2258

30

Metastatic NSCLC

Alectinib vs Crizotinib in UnRx ALK+ NSCLC

KEY ELIGIBILITY
- Advanced or metastatic *ALK*+ NSCLC
- *ALK*+ by central IHC testing
- Treatment-naïve
- ECOG PS 0–2
- Measurable disease
- Asymptomatic brain metastases allowed

RANDOMIZE
N=286

- **Alectinib** 600 mg BID PO
- *NO CROSSOVER* per protocol
- **Crizotinib** 250 mg BID PO

Stratification factors:
- ECOG PS (0/1 vs 2)
- Race (Asian vs non-Asian)
- Brain metastases (present vs absent)

ENDPOINTS
- Primary
  - PFS (RECIST 1.1), by investigator review
- Secondary
  - PFS by IRC
  - Time to CNS progression
  - ORR, DOR
  - OS
  - Safety and tolerability
  - Patient-reported outcomes

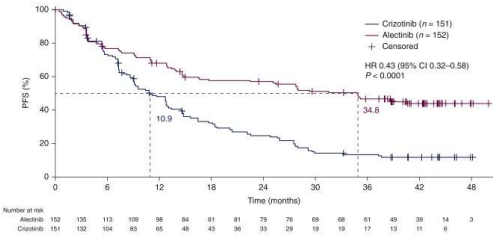
ALK, anaplastic lymphoma kinase; IHC, immunohistochemistry; NSCLC, non-small-cell lung cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PO, by mouth; PFS, progression-free survival; IRC, independent review committee; CNS, central nervous system; ORR, objective response rate; DOR, duration of response; OS, overall survival

Peters, et al. *NEJM*. 2017 377:829-838

31

Metastatic NSCLC

1st Gen ALK Inhibitor vs Alectinib in Untreated ALK+ NSCLC



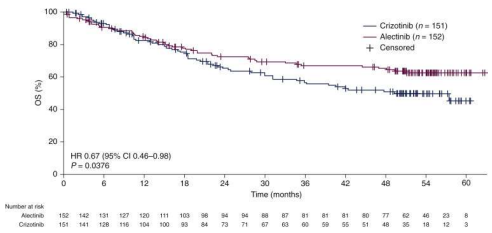
FDA APPROVED
2013
Crizotinib
ALK+ NSCLC
2017
Alectinib
unRx ALK+ NSCLC

Mok, et al. *Ann Oncol* 2020 Aug;31(8):1056

32

Metastatic NSCLC

1st Gen ALK Inhibitor vs Alectinib in UnRx ALK+ NSCLC



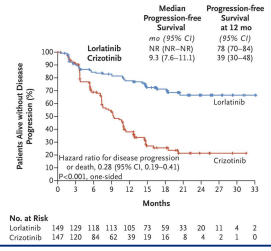
Mok, et al. *Ann Oncol* 2020 Aug;31(8):1056

33

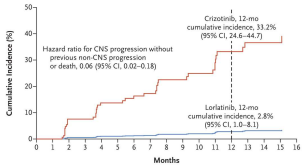
Metastatic NSCLC

Lorlatinib vs. Crizotinib for unRx ALK+ NSCLC

Progression-free Survival



Cumulative Incidence of CNS Progression as 1st Event



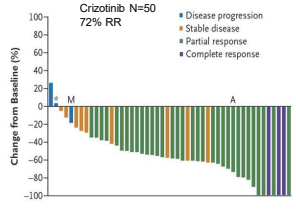
Shaw, et al. *New Engl J Med.* 2020 Nov 19;383(21):2018

34

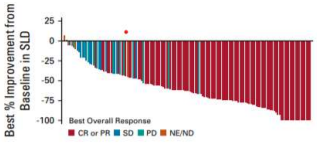
Metastatic NSCLC

ROS1+ NSCLC Rx with Crizotinib or Entrectinib

Crizotinib N=50
72% RR



Entrectinib N=108/161
67% RR



Shaw, et al. *NEJM.* 2014 371:1963

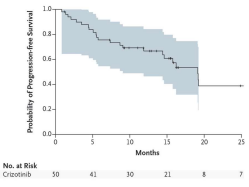
Dziadziuszko, et al. *J Clin Oncol.* 2021 Apr 10;39(11):1253

35

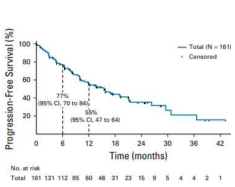
Metastatic NSCLC

ROS1+ NSCLC Rx with Crizotinib or Entrectinib

Crizotinib
PFS=19 Months



Entrectinib
PFS=16 months



FDA APPROVED
2016
Crizotinib
ROS1+ NSCLC
2019
Entrectinib
ROS1+ NSCLC

Shaw, et al. *NEJM.* 2014 371:1963

Dziadziuszko, et al. *J Clin Oncol.* 2021 Apr 10;39(11):1253

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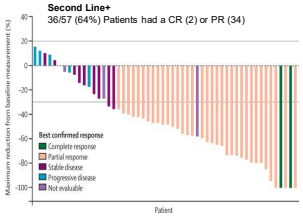
Metastatic NSCLC

RR of BRAF V600E NSCLC with Dabrafenib + Trametinib

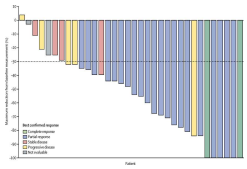
Progression-Free Survival of Approximately 10 months

Second Line+
36/57 (64%) Patients had a CR (2) or PR (34)



Planchard et al. *Lancet Oncol* 2016 Jul; 17(7):984-93

First Line
23/36 (64%) Patients had a CR (2) or PR (21)

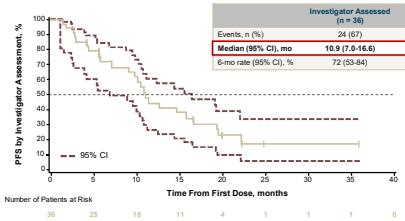


Planchard et al. *Lancet Oncol* 2017 18:1307

Metastatic NSCLC

BRAF V600E NSCLC Rx with Dabrafenib + Trametinib

Progression-free Survival



	Investigator Assessed (n = 36)	IRC Assessed (n = 36)
Events, n (%)	24 (67)	22 (61)
Median (95% CI), mo	**10.9 (7.0-16.6)**	**14.6 (7.0-22.1)**
6-mo rate (95% CI), %	72 (53-84)	69 (51-82)

FDA APPROVED

June 2017
Dabrafenib + Trametinib
Metastatic BRAF V600E NSCLC

Metastatic NSCLC

Additional Targeted Agent Single Arm US Approvals 2017-2021

Target	Drug	Response Rate	Duration Response	PFS
NTRK	Larotrectinib Entrectinib	75% 70%	35 Months 10 Months	28 Months 11 Months
RET	Selpercatinib Prasetinib	64% 58%	20 Months >11 Months	18 Months Not Eval
MET Exon 14	Capmatinib Tepotinib	48% 46%	11 Months 11 Months	10 Months 11 Months
EGFR Exon 20	Amivantinib	40%	10 months	8 Months
Median (Range)		**58 (40-75)**	**11 (10-35)**	**11 (8-28)**

Metastatic NSCLC

Sotorasib for KRAS G12C Mutant NSCLC

Patients with locally advanced or metastatic NSCLC

Key inclusion criteria
- ≥18 years*
- ECOG performance status 0 / 1
- KRAS G12C Mutation
- Previous Treatment with Checkpoint Inhibitor and/or Chemotherapy

Sotorasib
(960 mg p.o. qd)
(n=279)

RECIST 1.1 assessment until objective progressive disease or intolerable side effects,

Endpoints
- **Primary endpoint:** response rate based by independent assessment
- **Secondary endpoints:** duration of response, progression-free survival, and survival,

Soria, et al. *N Engl J Med.* 2018 Jan 11;378(2):113

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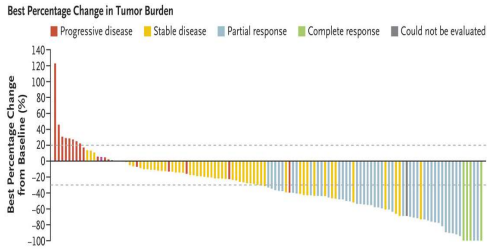
Metastatic NSCLC

Sotorasib for KRAS G12C Mutant NSCLC



Skoulidis, et al. New *Engl J Med* 2021 Jun 24;384(25):2371

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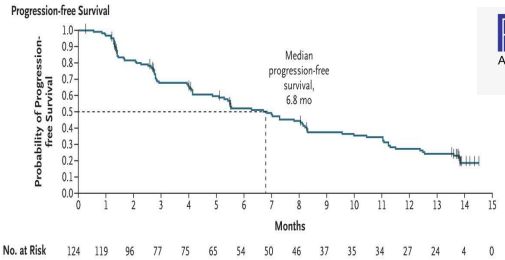
Metastatic NSCLC

Sotorasib for KRAS G12C Mutant NSCLC



FDA APPROVED
May 2021

Skoulidis, et al. New *Engl J Med* 2021 Jun 24;384(25):2371

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Stage III NSCLC

Management of Patients

Targeted Therapy (40%)

- NSCLC Pts with an EGFR mutation should be treated with Osimertinib
- NSCLC Pts with an ALK rearrangement should be treated with Alectinib
- NSCLC Pts with a ROS1 rearrangement should be treated with Crizotinib or Entretinib
- Patients with a V600E BRAF mutation should be treated with Dabrafenib plus Trametinib
- Patients with a RET rearrangement should be treated with Selpercatinib or Prasetinib
- Patients with an NTRK rearrangement should be treated with Larotrectinib or Entrectinib
- Patients with MET Exon14 mutation should be treated with Capmatinib or Tepotinib
- Patients with an Exon 20 Insertion Mutation of EGFR should be treated with Amivantinib
- Patients with a KRAS G12C mutation should be treated with sotorasib

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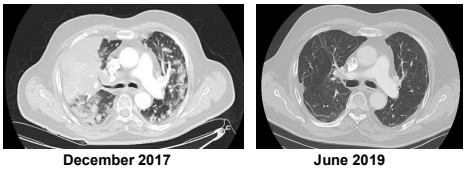
Metastatic NSCLC

Checkpoint Inhibitors as Single Agents

84-Year-Old Smoking Gentleman with Adenocarcinoma Treated on a Checkpoint Inhibitor as a Single Agent

PD-L1 >95% Tumor Mutational Burden/Megabase: 11.4



December 2017 June 2019

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Metastatic NSCLC

Pembrolizumab vs Chemotherapy in UnRx NSCLC

- NSCLC
- >50% PD-L1 Positive
- No Prior Therapy
- ECOG 0 or 1
- No Immune Disorders

RANDOMIZE*

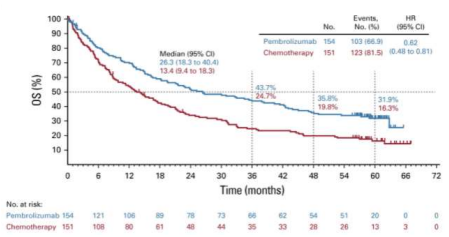
- Pembrolizumab 200 mg q 3 weeks
- Investigator Choice Platinum-Based Chemotherapy

Reck M, et al. *NEJM* 2016. Nov 10;375(19):1823

45

Metastatic NSCLC

Pembrolizumab vs Chemotherapy in UnRx NSCLC



FDA APPROVED
2016
Pembrolizumab
NSCLC & >50% PD-L1 Staining of Tumor Cells

Reck M, et al. *J Clin Oncol.* 2021 Jul 20;39(21):2339

Metastatic NSCLC

Pembrolizumab + Chemo vs Chemo in UnRx NSCLC

- NonSquamous NSCLC
- PD-L1 <1% versus PD-L1 >1%
- No Prior Therapy
- No EGFR or ALK
- ECOG 0 or 1
- No Rx for Immune Disorders

RANDOMIZE*

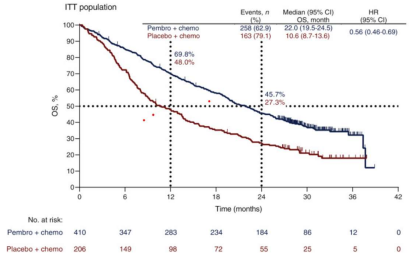
2 → **Pembrolizumab Plus Pemetrexed Platinum-Based Chemo**

1 → **Pemetrexed Platinum-Based Chemo**

Gandhi, et al. *NEJM.* 2018: May 31;378(22):2078

Metastatic NSCLC

Pembrolizumab + Chemo vs Chemo in UnRx NSCLC



FDA APPROVED
2018
Pembro + Pem/Carbo
Non-Squamous NSCLC

Rodríguez-Abreu D et al. *Ann Oncol.* 2021 Jul;32(7):881

Metastatic NSCLC

Pembro + Chemo vs Chemo in UnRx Squamous NSCLC

- Squamous NSCLC
- PD-L1 <1% versus PD-L1 >1%
- No Prior Therapy
- No EGFR or ALK
- ECOG 0 or 1
- No Rx for Immune Disorders

RANDOMIZE*

1 → Pembrolizumab Plus Paclitax/nab-Paclitax/Carbo

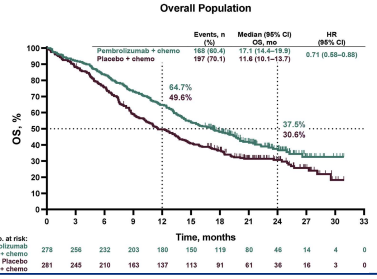
1 → Paclitax/Nab-Paclix/Carbo

Pas-Ares, et al. *N Engl J Med.* 2018 Nov 22;379(21):2040

Metastatic NSCLC

Pembro + Chemo vs Chemo in UnRx Squamous NSCLC

Overall Population



Pas-Ares, et al. *J Thorac Oncol.* 2020 Oct;15(10):1657

Metastatic NSCLC

Nivolumab-Ipilimumab for unRx NSCLC

Nivolimub plus Ipilimumab vs. Platinum-Based ChemoRx in previously untreated patients

- Squamous and NonSquamous Cell Lung Cancer
- No Prior Therapy regimen
- ECOG 0 or 1
- No EGFR Mutations or ALK Rearrangements
- No Immune Disorders

RANDOMIZE*

→ Nivo 3 mg/kg q 2 wks Ipi 1 mg/kg q 6 wks

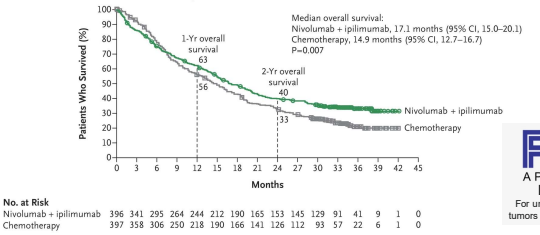
→ Platinum-Based Regimen q 3 wks

Hellman, et al. *NEJM.* 2019 381:2020

Metastatic NSCLC

Nivolumab-Ipilimumab for unRx NSCLC

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



FDA APPROVED
May 2020
For unRx patients whose tumors express PL-L1 ≥ 1%

Hellman, et al. *NEJM.* 2019 381:2020

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Metastatic NSCLC

Nivolumab-Ipilimumab-Chemo for unRx NSCLC

Nivolumab + Ipilimumab + 2 cycles of platinum-based chemo vs. chemo in untreated patients

- Squamous and NonSquamous Cell Lung Cancer
- No Prior Therapy regimen
- ECOG 0 or 1
- No EGFR Mutations or ALK Rearrangements
- No Immune Disorders

RANDOMIZE*

Nivo 3 mg/kg q 2 wks
Ipi 1 mg/kg q 6 wks
+ 2 Cycles Plat-Based Regimens q 3 wks

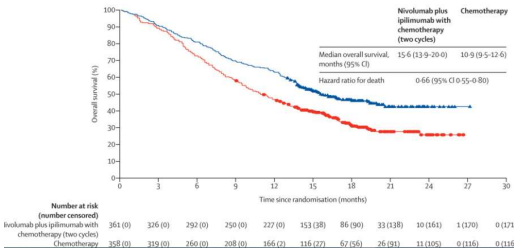
Platinum-Based Regimen q 3 wks

Paz Ares, et al. *Lancet Oncol.* 2021 Feb;22(2):198.

53

Metastatic NSCLC

Nivolumab-Ipilimumab-Chemo for unRx NSCLC



FDA APPROVED
May 2020

Paz Ares, et al. *Lancet Oncol.* 2021 Feb;22(2):198.

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Management of Untreated & Treated NSCLC

- Screening for Lung Cancer
- Adjuvant Therapy for Early Stage
- Chemotherapy with Surgery and Radiation in Locally Advanced Disease
- Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)

➤ **Relapsed Non-Small Cell Lung Cancer**

Relapsed NSCLC

Docetaxel vs Supportive Care

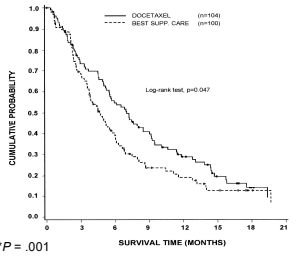
Patient characteristics

- Relapsed IIIB/IV NSCLC
- PS 0-2
- No prior paclitaxel therapy

BSC 100 pts vs. docetaxel (two doses) 104 pts.

Outcome measures

	Docetaxel	BSC
RR	5.8%	0%
TTP (weeks)	10.6*	6.7
OS (months)	7.0	4.6
1-year survival	29%	19%



*P = .001

Shepherd FA,, et al. *J Clin Oncol.* 000;18(10):2095-2103

Relapsed NSCLC

Nivolumab vs Docetaxel in Previously Rx Advanced Squamous-Cell NSCLC

- Squamous Cell Lung Cancer
- Prior Therapy with Platin-based regimen
- ECOG 0 or 1
- No Immune Disorders

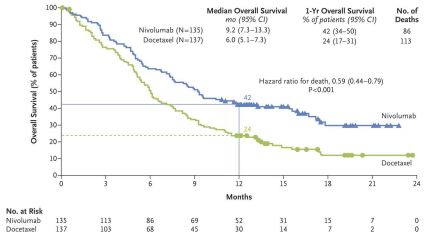
RANDOMIZE*

- **Nivolumab 3 mg/kg q 2 weeks**
- **Docetaxel 75 mg/m^2 q 3 weeks**

Brahmer, et al. *NEJM.* 2015; 373:123

Relapsed NSCLC

Nivolumab vs Docetaxel in Previously Rx Advanced Squamous-Cell NSCLC



Brahmer, et al. *NEJM*. 2015; 373:123

Relapsed NSCLC

Nivolumab vs Docetaxel in Advanced Squamous-Cell NSCLC

- NonSquamous NSCLC
- Prior Therapy with Platin-based regimen
- ECOG 0 or 1
- No Immune Disorders

RANDOMIZE*

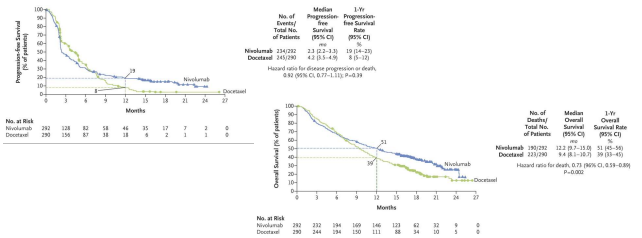
Nivolumab 3 mg/kg q 2 weeks

Docetaxel 75 mg/m² q 3 weeks

Borghaei H, et al. *NEJM*. 2015;373:1627

Relapsed NSCLC

Nivolumab vs Docetaxel in Previously Rx Advanced NonSquamous-Cell NSCLC

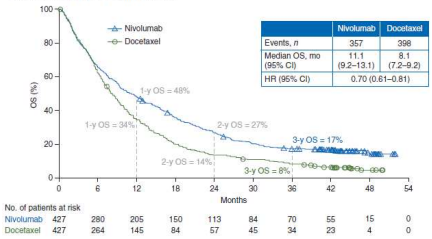


Borghaei H, et al. *NEJM*. 2015;373:1627

Relapsed NSCLC

Nivolumab vs Docetaxel in Previously Rx NSCLC

OS in Pooled CheckMate 017/057



	Nivolumab	Docetaxel
Events, *n*	357	398
Median OS, mo (95% CI)	11.1 (9.2–13.1)	8.1 (7.2–9.2)
HR (95% CI)	0.70 (0.61–0.81)	

Brahmer et al. *NEJM.* 2015; 373:123; Borghaei H, et al. *NEJM.* 2015;373:1627; Vokes EE, et al., *Ann Oncol.* 2018; Apr 1;29(4):959

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Relapsed NSCLC

Nivolumab vs Docetaxel in Advanced NSCLC

- NSCLC
- <1% PDL Positive
- Prior Therapy with Platin-based regimen
- ECOG 0 or 1
- No Immune Disorders

RANDOMIZE*

Pembrolizumab
2 mg/kg or 10 mg/kb
q 3 weeks

Docetaxel 75 mg/m²
q 3 weeks

Herbst et al. *Lancet* 2016; 387:1540

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Relapsed NSCLC

Management of Patients

Immunotherapy (60%)

- Patients with >50% PD-L1 staining in their tumor should be treated with pembrolizumab plus chemotherapy or pembrolizumab alone
- Patients with non-squamous NSCLC with PD-L1 staining of less than 50% should be treated with pembrolizumab plus pem/carbo
- *Patients squamous NSCLC with PD-L1 staining of less than 50% should be treated with pembrolizumab plus paclitaxel/nab-paclitaxel/carboplatin
- Patients with advanced NSCLC can be treated with 2 cycles of chemotherapy combined with nivolumab plus ipilimumab
- Patient who have not been treated with a checkpoint inhibitor as their initial therapy should be treated with a checkpoint inhibitor (nivolumab, pembrolizumab, or atezolizumab (pembro and atezo if PD-L1 is >1%)

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Management of Untreated & Treated NSCLC

- Screening for Lung Cancer
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- Current Standards and Studies for Metastatic NSCLC (Targeted Therapy-Immunotherapy)
- Relapsed Non-Small Cell Lung Cancer

Thank You