Overview of Adjuvant and Neoadjuvant Therapies: 2020-2021

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MONTEFIORE HEALTH SYSTEM – ALBERT EINSTEIN COLLEGE OF MEDICINE

Montefiore Einstein Cancer Center

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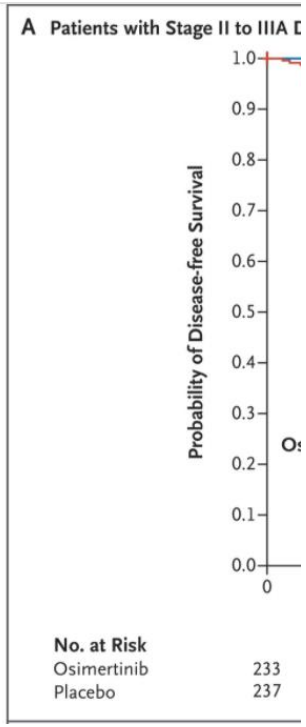
Board: Lung Cancer Research Foundation (pharma funding)

An evolving multidisciplinary landscape

- *Surgeons should lead*
- For early-stage patients (I-III), surgeons have the most comprehensive understanding of accuracy of staging, of surgical risk, of risk of disease recurrence, and of patient goals and values
- Several “game changers” in the adjuvant and neoadjuvant treatment paradigm in 2020-2021
- Molecular testing and PD-L1 status will increasingly be used to make a priori surgical treatment decisions

ADAURA: Adjuvant Osimertinib



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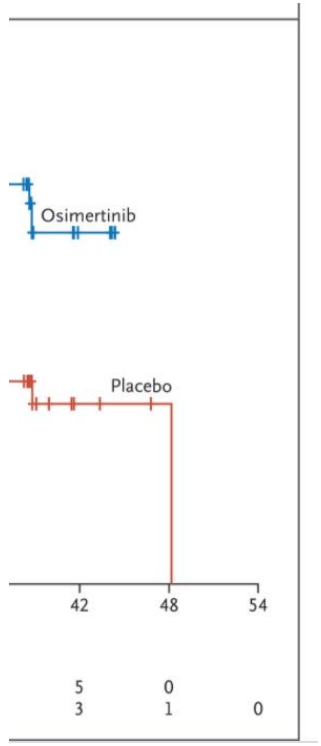
Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA Investigators*



N Engl J Med, 2020;383:1711-1723

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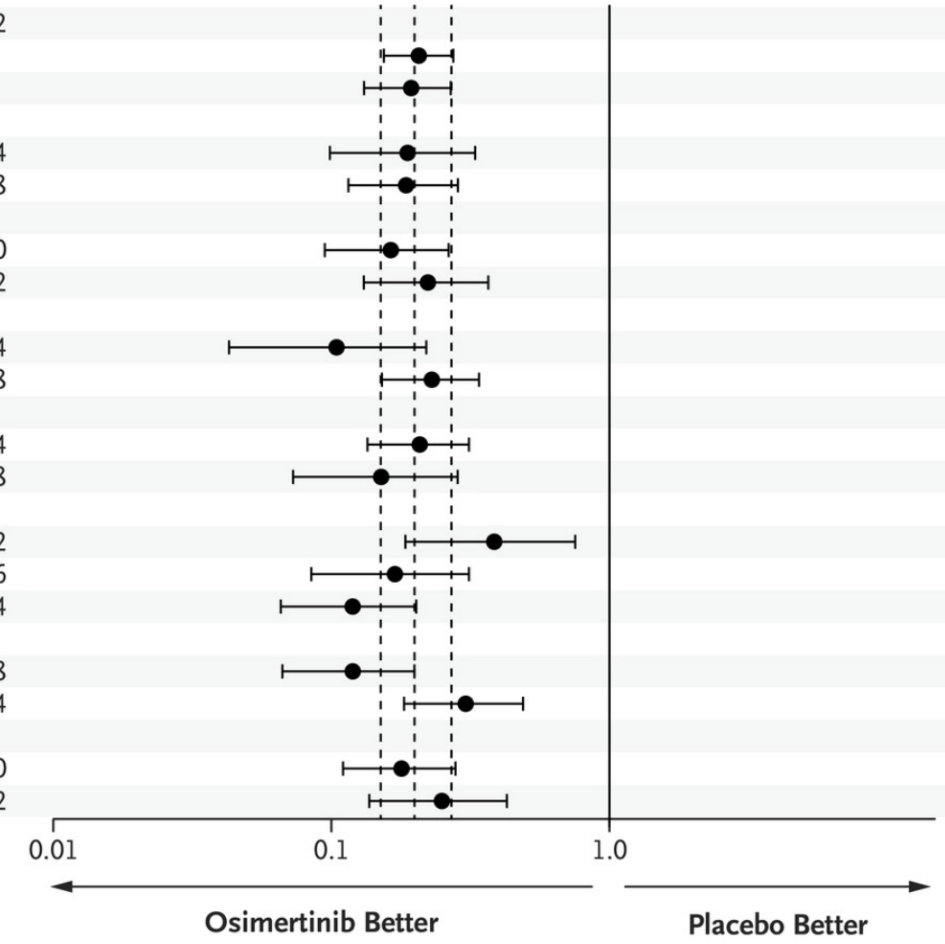
Efficacy across multiple subgroups

Subgroup	No. of Patients	Hazard Ratio for Disease Recurrence or Death (95% CI)
Overall	682	
Stratified log-rank test		0.20 (0.15–0.27)
Unadjusted Cox proportional-hazards model		0.19 (0.13–0.27)
Sex		
Male	204	0.19 (0.10–0.33)
Female	478	0.18 (0.11–0.28)
Age		
<65 yr	380	0.16 (0.09–0.26)
≥65 yr	302	0.22 (0.13–0.36)
Smoking history		
Yes	194	0.10 (0.04–0.22)
No	488	0.23 (0.15–0.34)
Race		
Asian	434	0.21 (0.13–0.31)
Non-Asian	248	0.15 (0.07–0.28)
Stage		
IB	212	0.39 (0.18–0.76)
II	236	0.17 (0.08–0.31)
IIIA	234	0.12 (0.07–0.20)
EGFR mutation		
Ex19del	378	0.12 (0.07–0.20)
L858R	304	0.31 (0.18–0.49)
Adjuvant chemotherapy		
Yes	410	0.16 (0.10–0.26)
No	272	0.23 (0.13–0.40)



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What to do with stage IB?

CLINICAL CANCER RESEARCH | CCR DRUG UPDATES

FDA Approval Summary: Osimertinib for Adjuvant Treatment of Surgically Resected Non–Small Cell Lung Cancer, a Collaborative Project Orbis Review

Abigail L. Koch[1], Paz J. Vellanki[1], Nicole Drezner[1], Xiaoxue Li[1], Pallavi S. Mishra-Kalyani[1], Yuan Li Shen[1], Huiming Xia[1], Yangbing Li[1], Jiang Liu[1], Jeanne Fourie Zirkelbach[1], Elitza Palazov[2], Aleksandr Gamarian[2], Qiuyi Choo[3], Arūnas Girčys[4], Ulrich-Peter Rohr[4], Nataliya Fesenko[1], Dianne Spillman[5], Richard Pazdur[1,5], Julia A. Beaver[1,5], and Harpreet Singh[1,5]

Table 1. DFS in ADAURA, per the seventh and eighth editions of the AJCC staging system.

	Stage IB		Stage II		Stage IIIA	
AJCC 7 (IVRS)[a]	**Osimertinib *N* = 106**	**Placebo *N* = 106**	**Osimertinib *N* = 118**	**Placebo *N* = 118**	**Osimertinib *N* = 115**	**Placebo *N* = 119**
Median, months (95% CI)[b]	NR (NE–NE)	48.2 (NE–NE)	NR (NE–NE)	29.4 (22.1–NE)	38.8 (34.3–NE)	12.7 (10.9–18.3)
HR (95% CI)[c]	0.39 (0.18–0.76)		0.17 (0.08–0.31)		0.12 (0.07–0.20)	
AJCC 8	**Osimertinib *N* = 50**	**Placebo *N* = 52**	**Osimertinib *N* = 78**	**Placebo *N* = 90**	**Osimertinib *N* = 62**	**Placebo *N* = 76**
Median, months (95% CI)[b]	NR (33.1–NE)	33.1 (21.0–NE)	NR (NE–NE)	28.1 (18.8–38.8)	38.8 (38.6–NE)	11.1 (9.7–16.5)
HR (95% CI)[c]	0.38 (0.17–0.84)		0.15 (0.07–0.33)		0.14 (0.07–0.27)	

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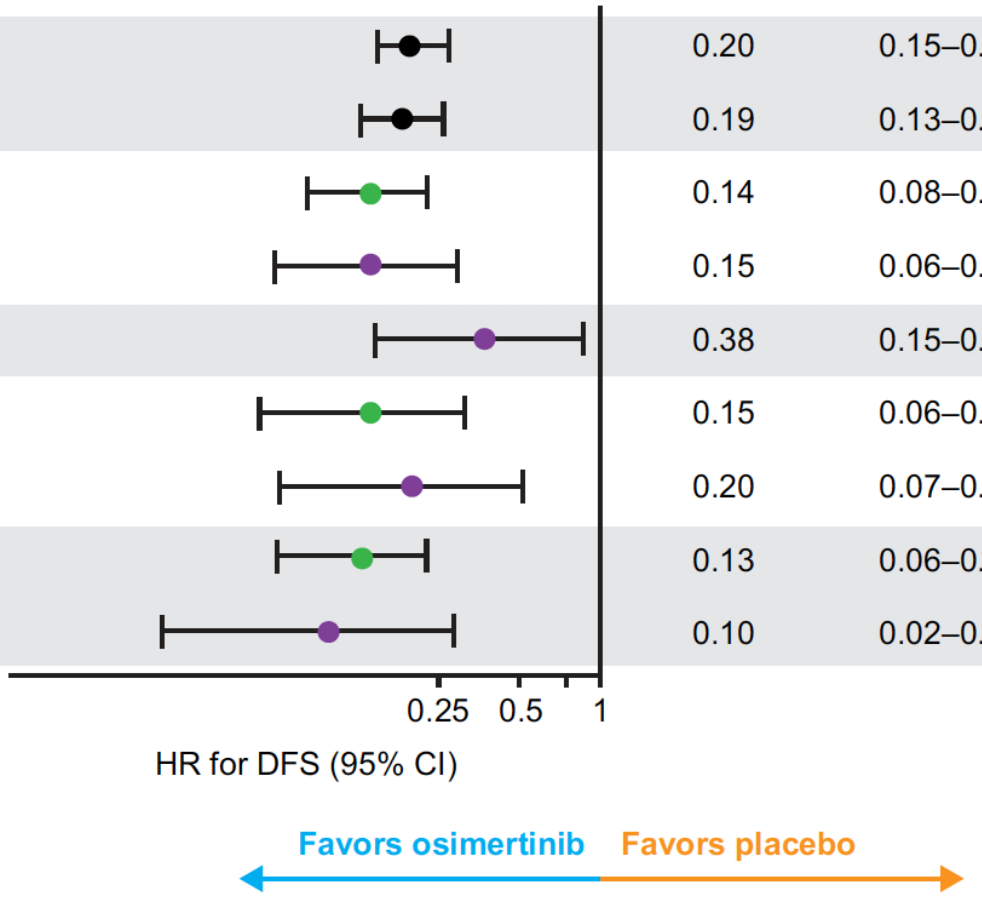
Adjuvant Osimertinib for Resected EGFRm NSCLC

Subgroup		HR	95% CI
Overall (N = 682)	Stratified log-rank	0.20	0.15–0.27
	Unadjusted Cox PH	0.19	0.13–0.27
Stage II / IIIA	With adjuvant chemotherapy (n = 352)	0.14	0.08–0.23
	Without adjuvant chemotherapy (n = 118)	0.15	0.06–0.30
Stage IB*	Without adjuvant chemotherapy (n = 154)	0.38	0.15–0.88
Stage II	With adjuvant chemotherapy (n = 166)	0.15	0.06–0.32
	Without adjuvant chemotherapy (n = 70)	0.20	0.07–0.52
Stage IIIA	With adjuvant chemotherapy (n = 186)	0.13	0.06–0.23
	Without adjuvant chemotherapy (n = 48)	0.10	0.02–0.29



- Overall population
- Patients with adjuvant chemotherapy
- Patients without adjuvant chemotherapy

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IMpower010 study design

Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB–IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial

*Enriqueta Felip, Nasser Altorki, Caicun Zhou, Tibor Csőszi, Ihor Vynnychenko, Oleksandr Goloborodko, Alexander Luft, Andrey Akopov, Alex Martinez-Marti, Hirotsugu Kenmotsu, Yuh-Min Chen, Antonio Chella, Shunichi Sugawara, David Voong, Fan Wu, Jing Yi, Yu Deng, Mark McCleland, Elizabeth Bennett, Barbara Gitlitz, Heather Wakelee, for the IMpower010 Investigators**

IC, tumor-infiltrating immune cells. [a] Per SP142 assay. [b] Two-sided α=0.05.

Published Online
September 20, 2021
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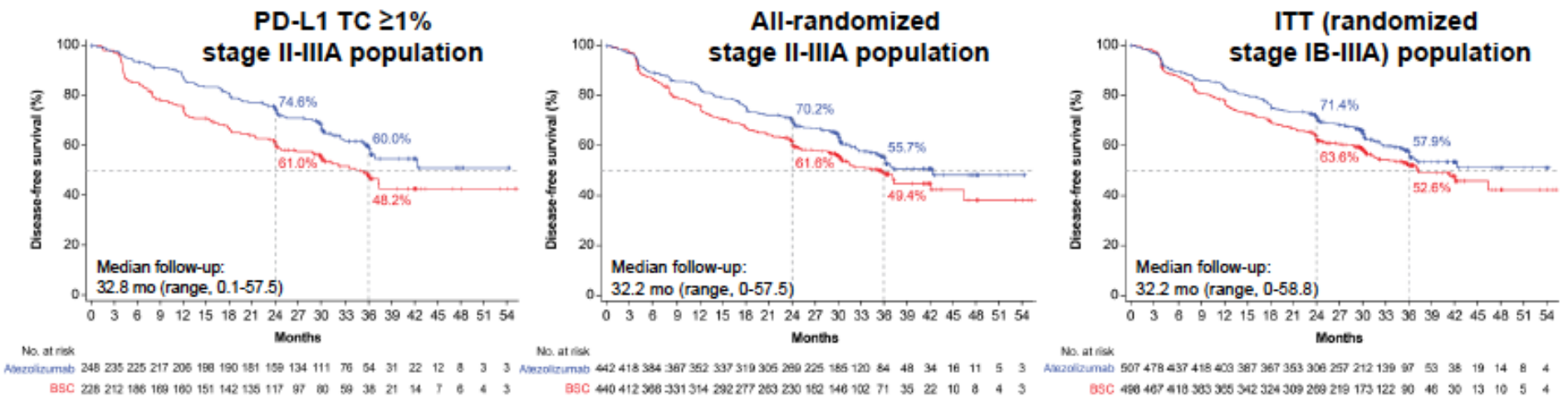
S0140-6736(21)02098-5

IIB	17.8%	%
IIIA	40.4%	41.8%

Dr. Heather A. Wakelee ASCO 2021, abstr 8500:IMpower010 Interim Analysis; https://bit.ly/33t6JJ; Felip Lancet 2021

IMPOWER010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA, all-randomized stage II-IIIA and ITT populations (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]	

	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	

	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[d]	

Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS. [d] The statistical significance boundary for DFS was not crossed.

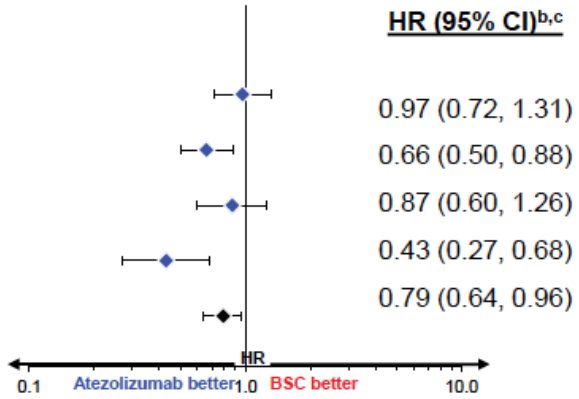
Dr. Heather A. Wakelee ASCO 2021, abstr 8500:IMpower010 Interim Analysis; https://bit.ly/33t6JJ; Felip Lancet 2021

Does PD-L1 matter?

DFS by PD-L1 status[a]

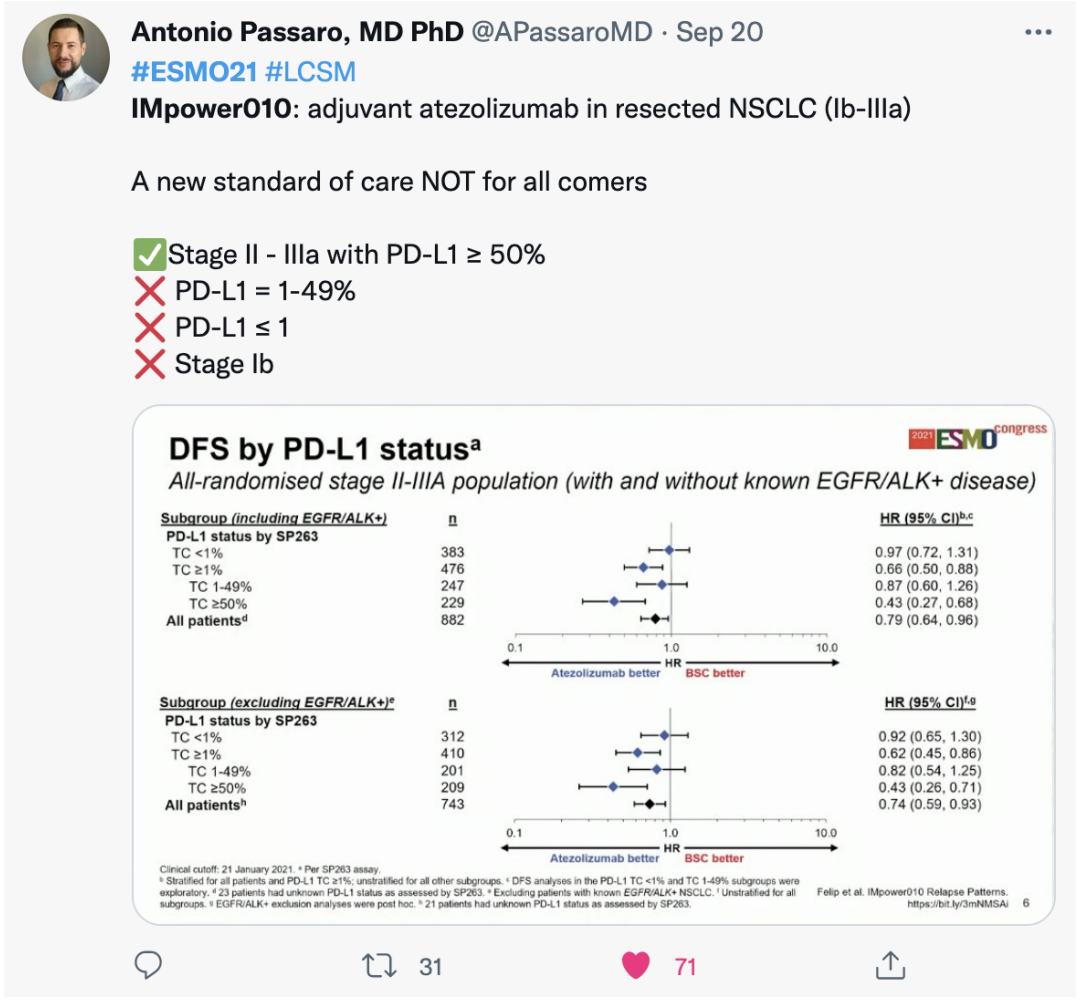
All-randomised stage II-IIIA population (with and without known EGFR/ALK+ disease)

Subgroup *(including EGFR/ALK+)*	n	HR (95% CI)[b,c]
PD-L1 status by SP263		
TC <1%	383	0.97 (0.72, 1.31)
TC ≥1%	476	0.66 (0.50, 0.88)
TC 1-49%	247	0.87 (0.60, 1.26)
TC ≥50%	229	0.43 (0.27, 0.68)
All patients[d]	882	0.79 (0.64, 0.96)



Clinical cutoff: 21 January 2021. [a] Per SP263 assay.
[b] Stratified for all patients and PD-L1 TC ≥1%; unstratified for all other subgroups. [c] DFS analyses in the PD-L1 TC <1% and TC 1-49% subgroups were exploratory. [d] 23 patients had unknown PD-L1 status as assessed by SP263. [e] Excluding patients with known *EGFR/ALK+* NSCLC. [f] Unstratified for all subgroups. [g] EGFR/ALK+ exclusion analyses were post hoc. [h] 21 patients had unknown PD-L1 status as assessed by SP263.

Felip ESMO2021



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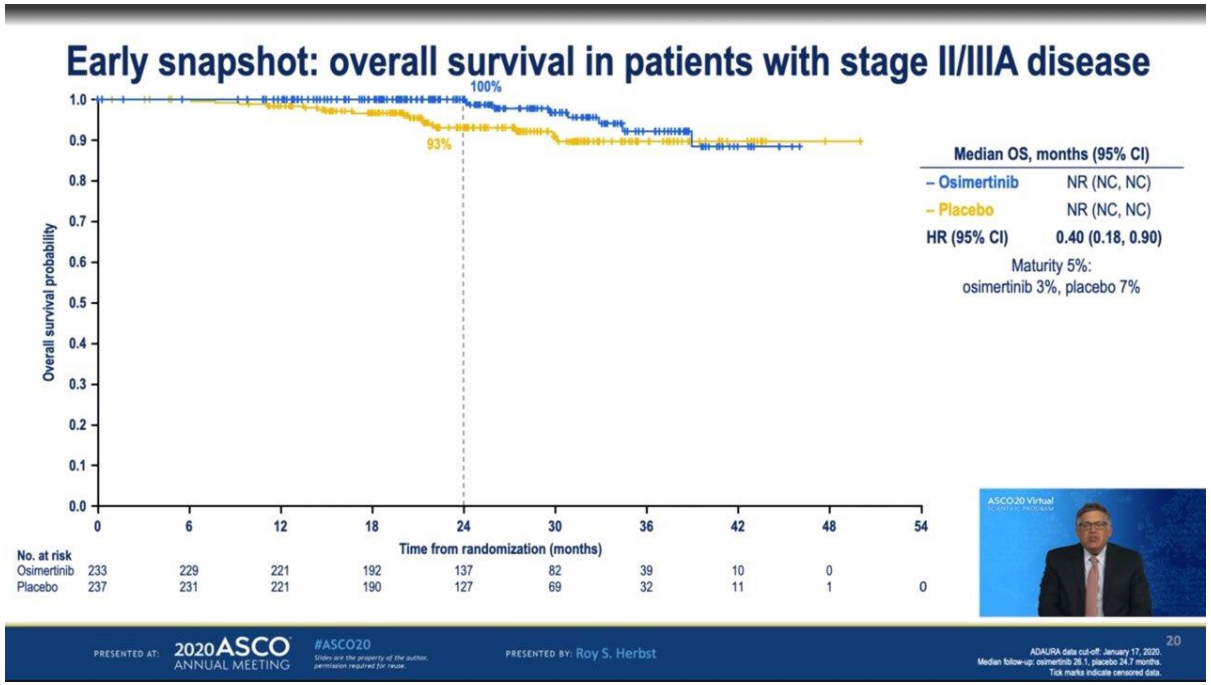
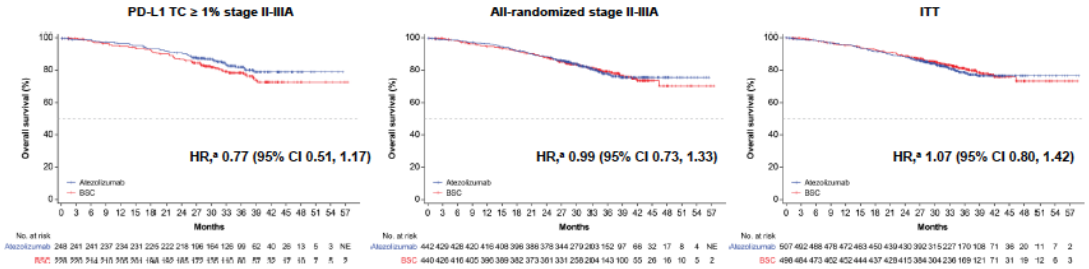
We still need to see how adjuvant therapy changes OS



IMpower010: early OS data at interim- Exploratory 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: January 21, 2021. ▪ Stratified.

Dr. Heather A. Wakelee ASCO 2021, abstr 8500:IMpower010 Interim Analysis; https://bit.ly/33t6JJ; Felip Lancet 2021

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A lot more data (and more potential options) on the way

Adjuvant PD-1/PD-L1 IO trials

Drug/Trial	Description	Stages entered	Description	Primary endpoint
Nivolumab	US, NCI (ECOG), Observational control	IB (4cm)-IIIA After Adj Chemo +/- radiation	Phase 3 Allows PD-L1 +/-	OS/DFS
Atezolizumab	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Durvalumab	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Pembrolizumab PEARLS KN-091	ETOP/EORTC, Placebo Controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS

PEARLS / KN-091 Press Release

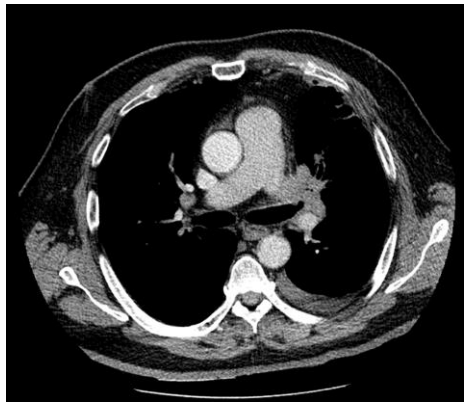
PRESS RELEASE JANUARY 10, 2022:

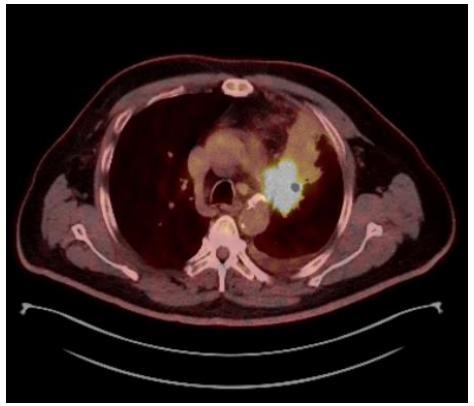
Adjuvant treatment with pembrolizumab led to a **statistically significant improvement in DFS** vs placebo in patients with stage **IB to IIIA** NSCLC following resection, **regardless of PD-L1 expression**, meeting 1 of the dual primary end points of the trial.

Additional results from the interim analysis showed that pembrolizumab also resulted in an **improved DFS** compared with placebo in those whose tumors did express **PD-L1** with a tumor proportion score (TPS) of **50% or higher**; however, this was **not found to meet statistical significance** per the prespecified statistical plan for the trial. !!!!!!!!!!!!

Neoadjuvant immunotherapy: The foundation trials

Study	Stage	N	Backbone	Published	MPR/CPR	Percent undergoing resection
JHU/MSKCC	IB-IIIA	21	Nivo x 2	NEJM 2018	45% / 15%	20 (95%)
NEOSTAR	I-IIIA	23 21	Nivo x 2 Nivo/Ipi	Nat Med 2021	17% / 9% 33% / 29%	39 (89%)
LCMC3	IB-IIIA	101	Atezo x 2	-	19% / 5%	90 (89%)
Weill Cornell	IB-IIIA	60	Durva x 2 Durva + SBRT x 2	Lancet Oncol 2021	6.7% / 0 53% / 31%	52 (87%)
Columbia / MGH	IB-IIIA	30	Atezo + carbo/tax	Lancet Oncol 2020	57% / 33%	29 (97%)
NADIM	IIIA	46	Nivo + carbo/tax	Lancet Oncol 2020	83% / 63%	41 (89%)





Duke: IB-IIIA, Neoadjuvant pembro, n=30, JTCVS

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CheckMate 816: Neoadjuvant nivolumab + chemotherapy

AACR American Association for Cancer Research

Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer in the phase 3 CheckMate 816 trial

Patrick M. Forde,[1] Jonathan Spicer,[2] Shun Lu,[3] Mariano Provencio,[4] Tetsuya Mitsudomi,[5] Mark M. Awad,[6] Enriqueta Felip,[7] Stephen Broderick,[1] Julie Brahmer,[1] Scott J. Swanson,[6] Keith Kerr,[8] Changli Wang,[9] Gene B. Saylors,[10] Fumihiro Tanaka,[11] Hiroyuki Ito,[12] Ke-Neng Chen,[13] Cecile Dorange,[14] Junliang Cai,[14] Joseph Fiore,[14] Nicolas Girard[15]

[1]Johns Hopkins Kimmel Cancer Center, Baltimore, MD, USA; [2]McGill University Health Center, Montreal, Québec, Canada; [3]Shanghai Chest Hospital, Shanghai, China; [4]Hospital Universitario Puerta de Hierro, Madrid, Spain; [5]Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [8]Aberdeen Royal Infirmary, Aberdeen, UK; [9]Tianjin Lung Cancer Center, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [10]Charleston Oncology, Charleston, SC, USA; [11]University of Occupational and Environmental Health, Kitakyushu, Japan; [12]Kanagawa Cancer Center, Yokohama, Japan; [13]Peking University School of Oncology, Beijing Cancer Hospital, Beijing, China; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]Institut du Thorax Curie-Montsouris, Institut Curie, Paris, France

Presentation Number CT003

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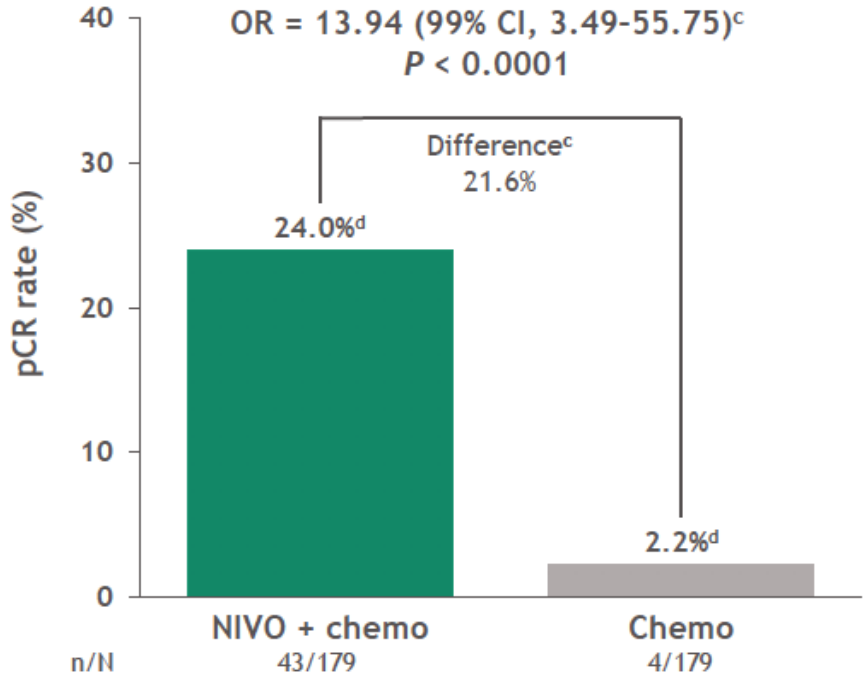
Pathological response

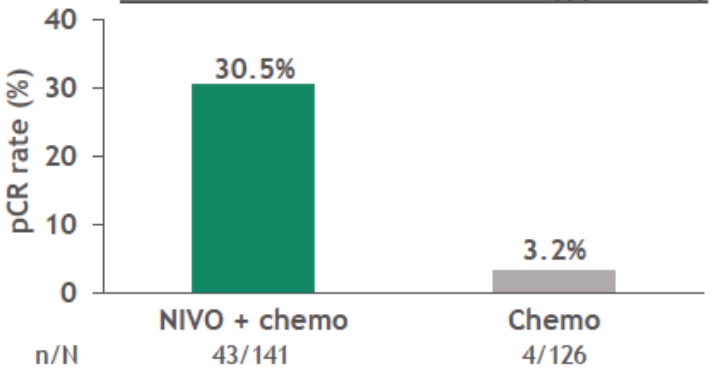
CheckMate 816: pCR with neoadjuvant NIVO + chemo in resectable NSCLC

Primary endpoint: pCR[a] rate with neoadjuvant NIVO + chemo vs chemo

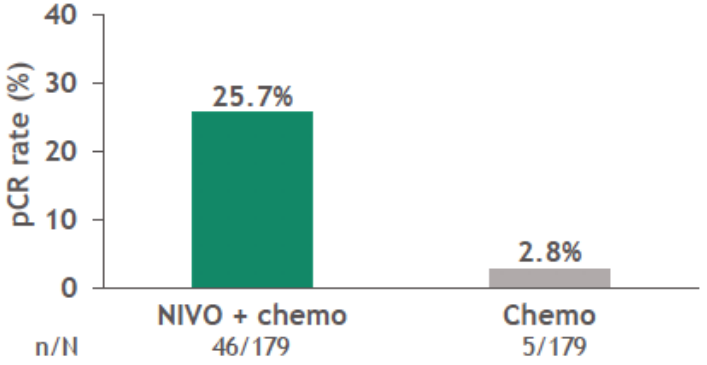
Primary endpoint: ITT (ypT0N0)[b]



Patients with resection[e] (ypT0N0)



Primary tumor only in ITT (ypT0)



- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)

[a]Per BIPR; pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]ITT principle: patients who did not undergo surgery counted as non-responders for primary analysis; [c]Calculated by stratified Cochran-Mantel-Haenszel method; [d]pCR rates 95% CI: NIVO + chemo, 18.0-31.0; chemo, 0.6-5.6; [e]Patients who underwent definitive surgery with an evaluable pathology sample for BIPR.

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MPR 37% NIVO/chemo vs. 9% chemo

Median viable tumor cells, 10% NIVO/chemo vs. 74% chemo

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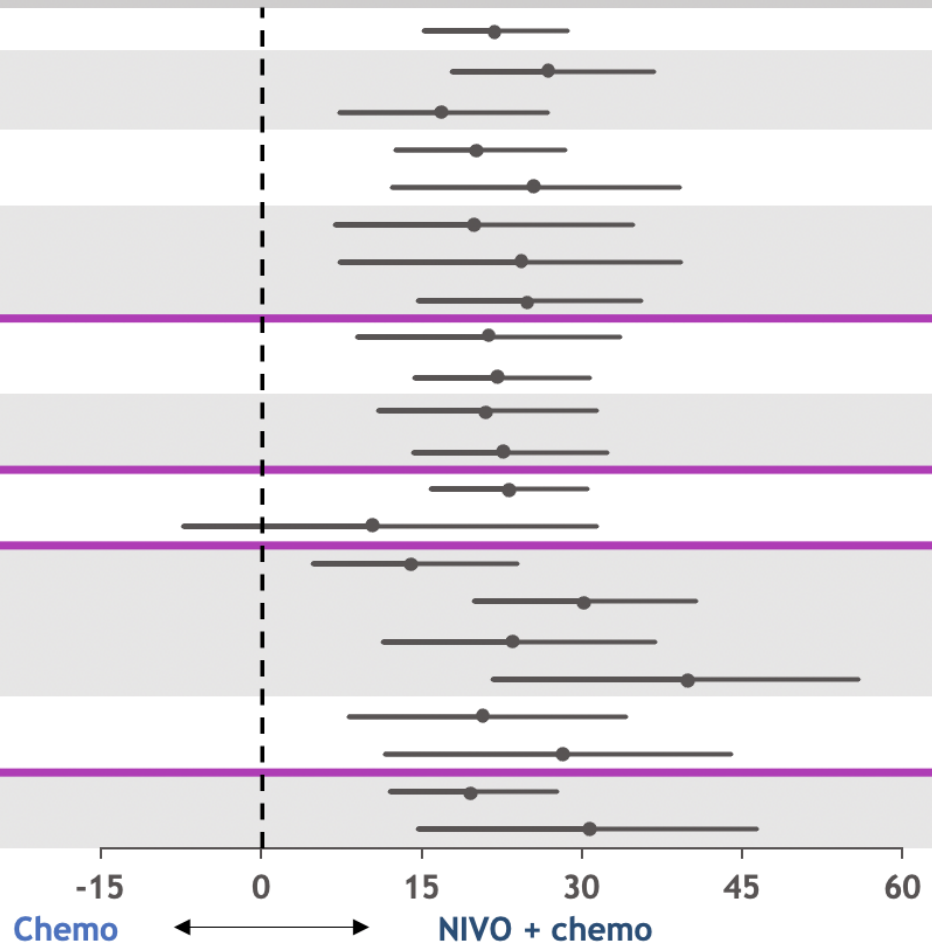
Checkmate 816

pCR* rate was higher with neoadjuvant nivolumab + chemo vs chemo across key subgroups

	pCR rate, %		Unweighted pCR difference, % (95% CI)	Unweighted pCR difference, %
	NIVO + chemo (n = 179)	Chemo (n = 179)		
Overall (N = 358)	**24**	**2**		22
< 65 years (n = 176)	27	0		27
≥ 65 years (n = 182)	21	4		17
Male (n = 255)	23	2		20
Female (n = 103)	28	2		26
North America (n = 91)	22	2		20
Europe (n = 66)	24	0		24
Asia (n = 177)	28	3		25
Stage IB–II (n = 128)	**26**	**5**		**21**
Stage IIIA (n = 228)	**23**	**1**		**22**
Squamous (n = 182)	**25**	**4**		**21**
Non-squamous (n = 176)	**23**	**0**		**23**
Current/former smoker (n = 318)	26	2		23
Never smoker (n = 39)	10	0		10
PD-L1 < 1% (n = 155)	**17**	**3**		**14**
PD-L1 ≥ 1% (n = 178)	**33**	**2**		**30**
PD-L1 1–49% (n = 98)	24	0		24
PD-L1 ≥ 50% (n = 80)	45	5		40
TMB < 12.3 mut/Mb (n = 102)	22	2		21
TMB ≥ 12.3 mut/Mb (n = 76)	31	3		28
Cisplatin (n = 258)	22	2		20
Carboplatin (n = 72)	31	0		31



Subgroup analyses are only descriptive and should be interpreted with caution.

*Per BIPR in ITT.

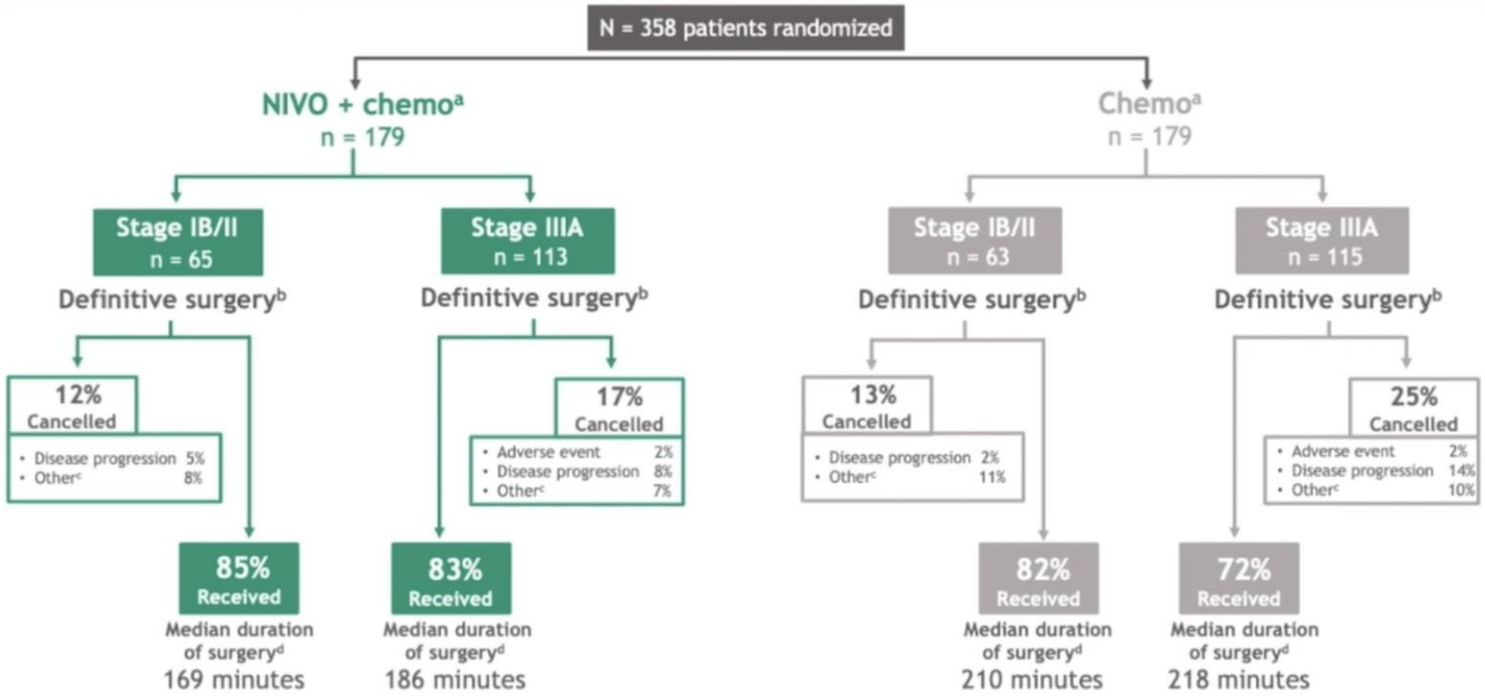
Forde PM et al. Oral presentation at AACR 2021. Abstract CT003.

What does that mean for us?
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Surgery summary: by baseline stage of disease



[a]1 patient with stage IV in each arm; [b]Patients with definitive surgery not reported: NIVO + chemo, 3% (stage IB/II), 0 (stage IIIA); chemo, 5% (stage IB/II), 3% (stage IIIA); [c]Other reasons included patient refusal, unresectability, and poor lung function; [d]Patients (n) with reported duration of surgery: NIVO + chemo, 46 (stage IB/II), 76 (stage IIIA); chemo, 47 (stage IB/II), 74 (stage IIIA); IQR for median duration of surgery: NIVO + chemo, 126.0-275.0 (stage IB/II) and 134.5-245.5 (stage IIIA); chemo, 150.0-267.0 (stage IB/II) and 147.0-290.0 (stage IIIA).

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2021 ASCO ANNUAL MEETING

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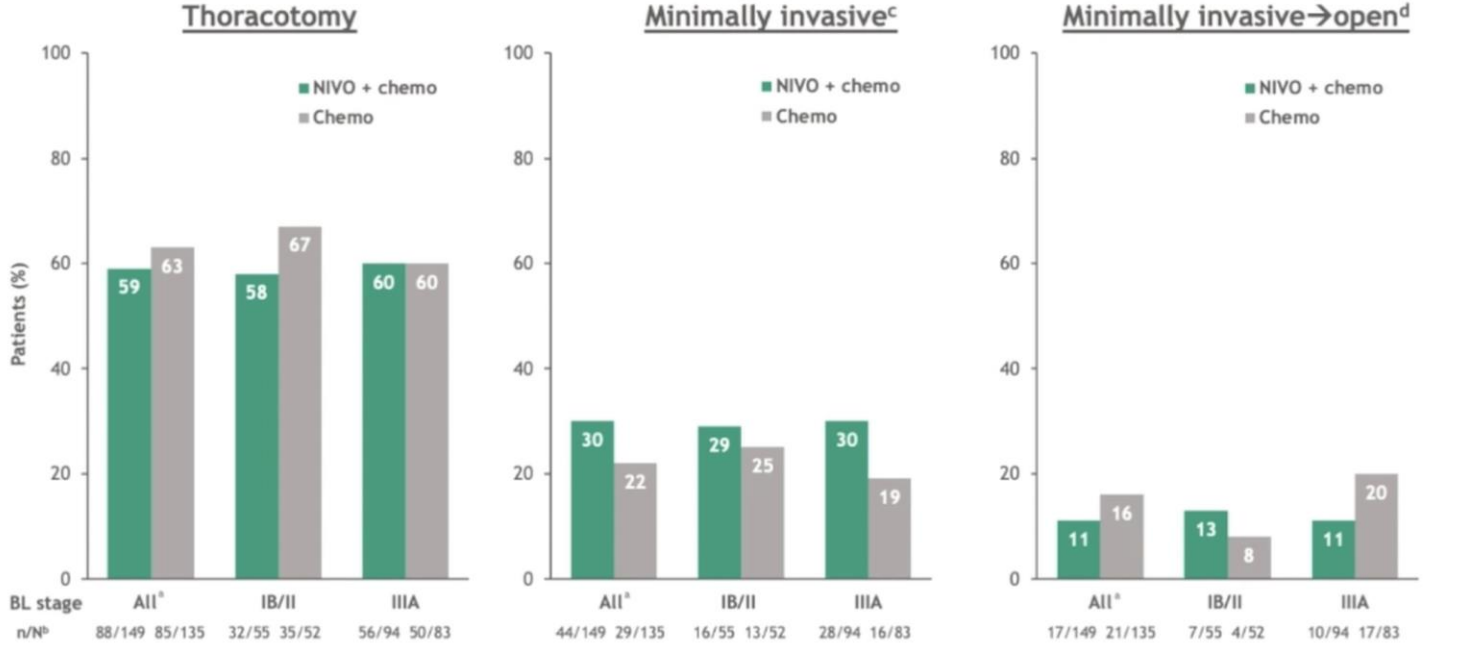
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Surgical approach by baseline stage of disease



[a]Patients with all baseline stages of disease and definitive surgery; [b]Denominator based on patients with definitive surgery; [c]Thoracoscopic/robotic; [d]Minimally invasive to thoracotomy.

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Jonathan Spicer, MD
Division of General Surgery,
McGill University Health Center,
Montreal, Quebec
Canada

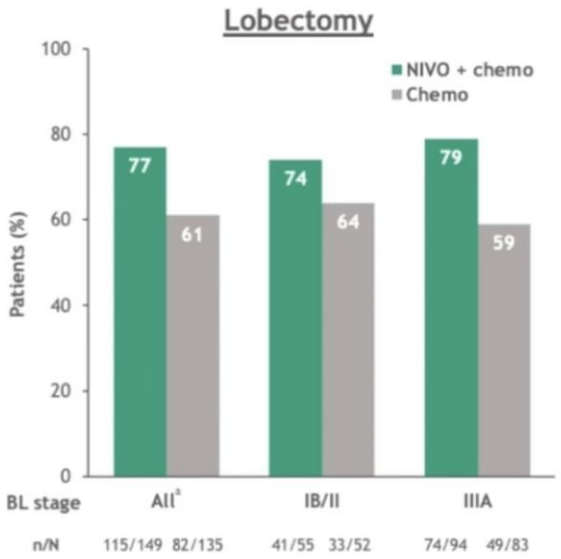
2021 ASCO ANNUAL MEETING

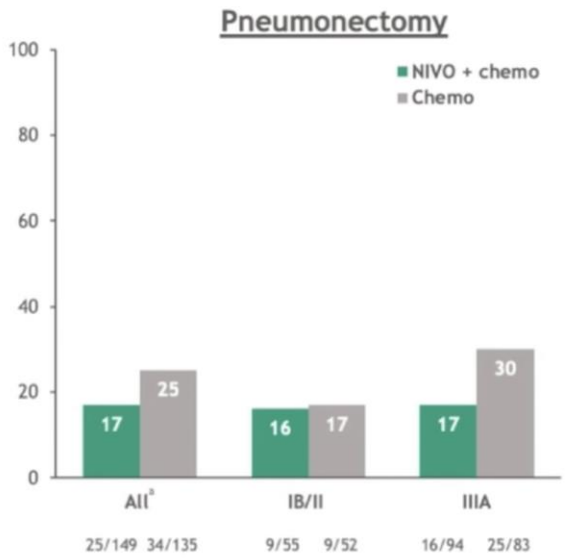
IMPROVED surgical outcomes

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

CheckMate 816: surgical outcomes with neoadjuvant NIVO + chemo in resectable NSCLC

Type of surgery by baseline stage of disease





Patients may have had > 1 surgery type. Patient numbers (n/N) for stage IB/II and stage IIIA, respectively, for bilobectomy (NIVO + chemo: 1/55, 2/94; chemo: 2/52, 2/83), sleeve lobectomy (NIVO + chemo: 2/55, 0/94; chemo: 5/52, 5/83), and other (NIVO + chemo: 13/55, 11/94; chemo: 12/52, 9/83). [a]Patients with all baseline stages of disease with surgery.

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2021 ASCO ANNUAL MEETING

And just last week…

Patrick Forde
@FordePatrick

Chemo-immunotherapy for earlier stage lung cancer approved! 8yrs have flown since our 1st trial of neoadj nivo began, thanks to many incl @SU2C @AACR @bmsnews @LUNGevity Most of all pts with a leap of faith to take part in cancer trials, this is for you!

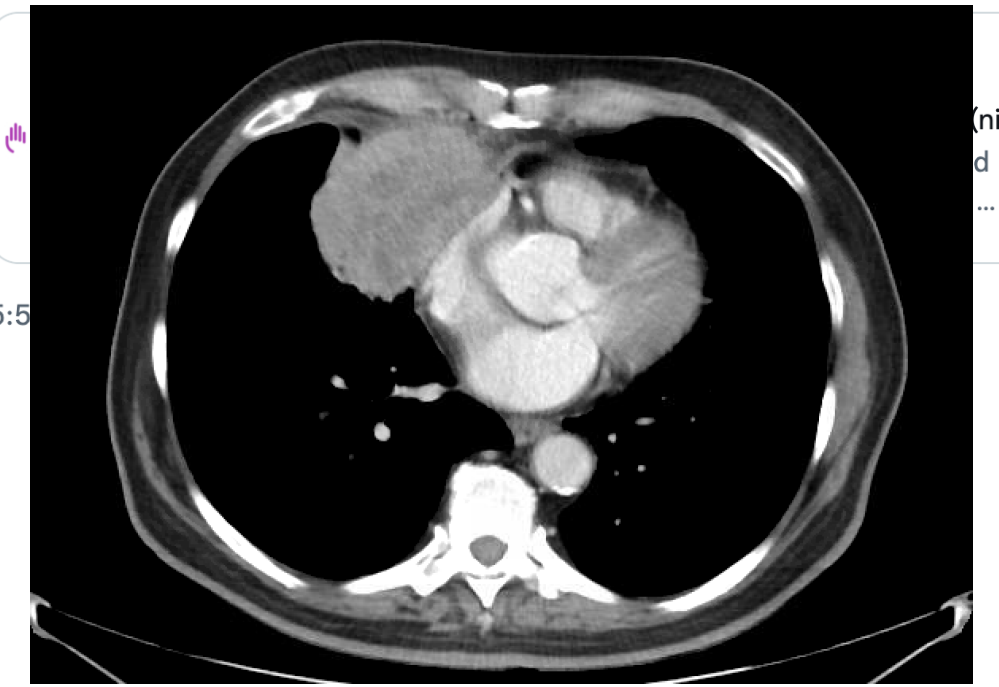

Figure 5: Event-Free Survival - CHECKMATE-816

Table 48: Efficacy Results - CHECKMATE-816

	OPDIVO and Platinum-Doublet Chemotherapy (n=179)	Platinum-Doublet Chemotherapy (n=179)
Event-free Survival (EFS) per BICR		
Events (%)	64 (35.8)	87 (48.6)
Median (months)[a] (95% CI)	31.6 (30.2, NR)	20.8 (14.0, 26.7)
Hazard Ratio[b] (95% CI)	0.63 (0.45, 0.87)	
Stratified log-rank p-value[c]	0.0052	
Pathologic Complete Response (pCR) per BIPR		
Number of patients with pCR	43	4
pCR Rate (%), (95% CI)[d]	24.0 (18.0, 31.0)	2.2 (0.6, 5.6)
Estimated treatment difference (95% CI)[e]	21.6 (15.1, 28.2)	
p-value[f]	<0.0001	

At the time of the EFS analysis, 26% of the patients had died. A prespecified interim analysis for OS resulted in a HR of 0.57 (95% CI: 0.38, 0.87), which did not cross the boundary for statistical significance.

Montefiore Einstein Cancer Center

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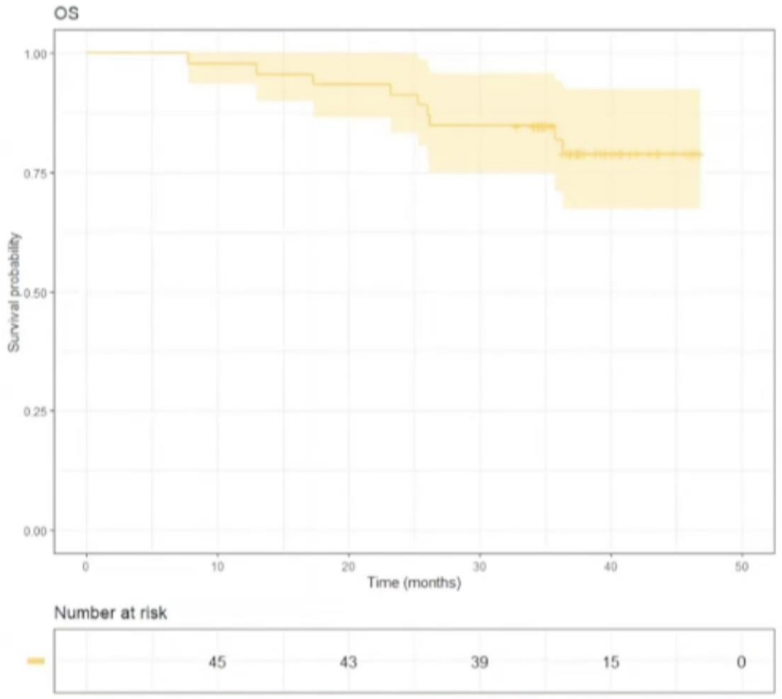
Will this set a new standard for OS for locally advanced NSCLC?

Long Term Survival in Operable Stage Iiia Nsclc Patients Treated With Neoadjuvant Nivolumab Plus Chemotherapy - Nadim Study

IASLC

2021 World Conference on Lung Cancer

RESULTS: OS



ITT population:

- **OS 81.9%** (95% CI: 66.8-90.6%) **at 36 months.**
- **OS 78.9%** (95%CI: 63.1-88.6%) **at 42 months.**

PP population:

- **OS 91.0%** (95%CI: 74.2-97.0%) **at 36 months.**
- **OS 87.3%** (95%CI: 69.3-95.1%) **at 42 months.**

Mariano Provencio MD, PhD

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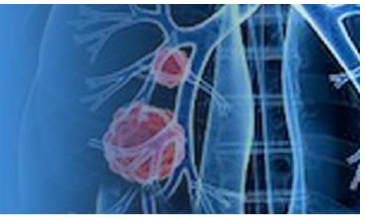
Lots more data on the way

Ongoing Phase III Trials of Neoadjuvant Chemotherapy Plus PD-1/PD-L1 Antibody in NSCLC



PD-1/PD-L1 Antibody	Trial (Estimated Enrollment)	Stage (AJCC ed)	Backbone	Neoadjuvant IO Intervention	Adjuvant IO Intervention	Primary Endpoints
Nivolumab	CheckMate 816[1] (N = 350)	IB–IIIA (7^{th})	Platinum-doublet chemotherapy	+/- Nivolumab IPI + NIVO (closed)	No	pCR EFS
	CheckMate 7TT[2] (N = 452)	II–IIIB (8^{th})	Platinum-doublet chemotherapy	Nivolumab or placebo	Nivolumab or placebo	EFS
Pembrolizumab	KEYNOTE-671[3] (N = 786)	IIA–IIIB (8^{th})	Platinum-doublet chemotherapy	Pembrolizumab or placebo	Pembrolizumab or placebo	EFS OS
Atezolizumab	IMpower030[4] (N = 450)	II–IIIB (8^{th})	Platinum-doublet chemotherapy	Atezolizumab or placebo	Atezolizumab or BSC	EFS
Durvalumab	AEGEAN[6] (N = 800)	IIA-IIIB (8^{th})	Platinum-doublet chemotherapy	Durvalumab or placebo	Durvalumab or placebo	pCR EFS

Dr. Patrick Forde, Targeted Therapies of Lung Cancer, 2022

The future of targeted therapy

- Multiple a
  - ALCH
  - ADAU
  - LAUR
  - ALK,
- Will conti testing ea process
- Role of lic residual c

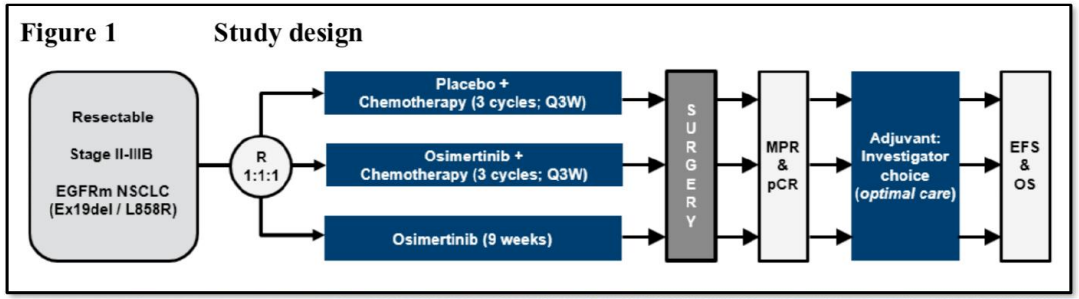
LCRF LEADER

Neoadjuvant Screening Trial: LCMC4

Evaluation of **A**ctionable **D**rivers in **E**a**R**ly Stage Lung Cancer

Neo/Adjuvant Trials

- Neo-ADAURA: Phase II, osimertinib vs chemotherapy vs the combination
- NAUTIKA1: Phase II, Neoadjuvant and Adjuvant Study of Alectinib, Entrectinib, Vemurafenib Plus Cobimetinib, or Pralsetinib in Patients With Resectable Stages II-III Non-Small Cell Lung Cancer With ALK, ROS1, NTRK, BRAF V600, or RET Molecular Alterations
- Geometry N: Phase II Study of Neoadjuvant and Adjuvant Capmatinib in NSCLC



Goldman, UCLA, USA

Montefiore Einstein Cancer Center

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Which strategy?
Advantages of neoadjuvant therapy

- *"Improved patient tolerance prior to surgery"*
- *"Tumor downstaging"*
- *"An earlier opportunity to eradicate micrometastases"*
- *"More rapid assessment of therapeutic efficacy"*
- *"Theoretical advantage of of improved efficacy to immunotherapy with the tumor in situ"*
- *"Permitting a change in systemic treatment"*
- *"Opportunity to evaluate surrogate markers of clinical efficacy"*

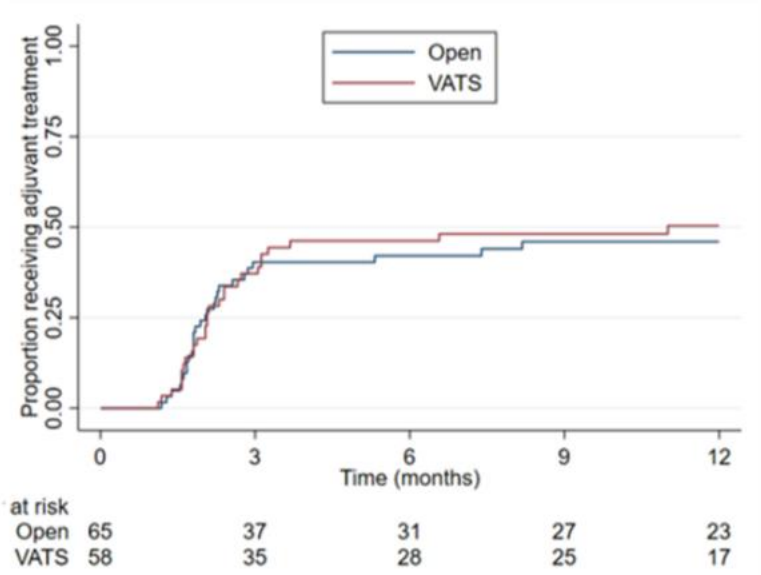
Chaft et al., Evolution of systemic therapy for stages I-III non-metastatic non-small-cell lung cancer. *Nat Rev Clin Oncol*, 2021;18(9):547-557

Low rates of adjuvant uptake: VIOLET

Outcome	Randomised to VATS (n=247)	Randomised to open surgery (n=255)	HR (95% CI)	p value
Received adjuvant treatment	34/216 (15.7%)	39/216 (18.1%)		
Received adjuvant treatment (eligible subset [a])	28/55 (50.9%)	28/61 (45.9%)		
Time to uptake of adjuvant treatment (months)	-	-	HR=0.90 (0.50, 1.61)	0.716
Time to uptake of adjuvant treatment (eligible subset [a]) (months)	11.0 (2.1, -)	- (2.0, -)	HR=1.12 (0.62, 2.02)	0.716

Data are n/N (%). Analyses are adjusted for operating surgeon.

a Eligible if i) N1-2 disease and M0 disease after surgery, or ii) T2b to 4, N0 and M0 after surgery.



Median (IQR) time to adjuvant treatment (months) for eligible:

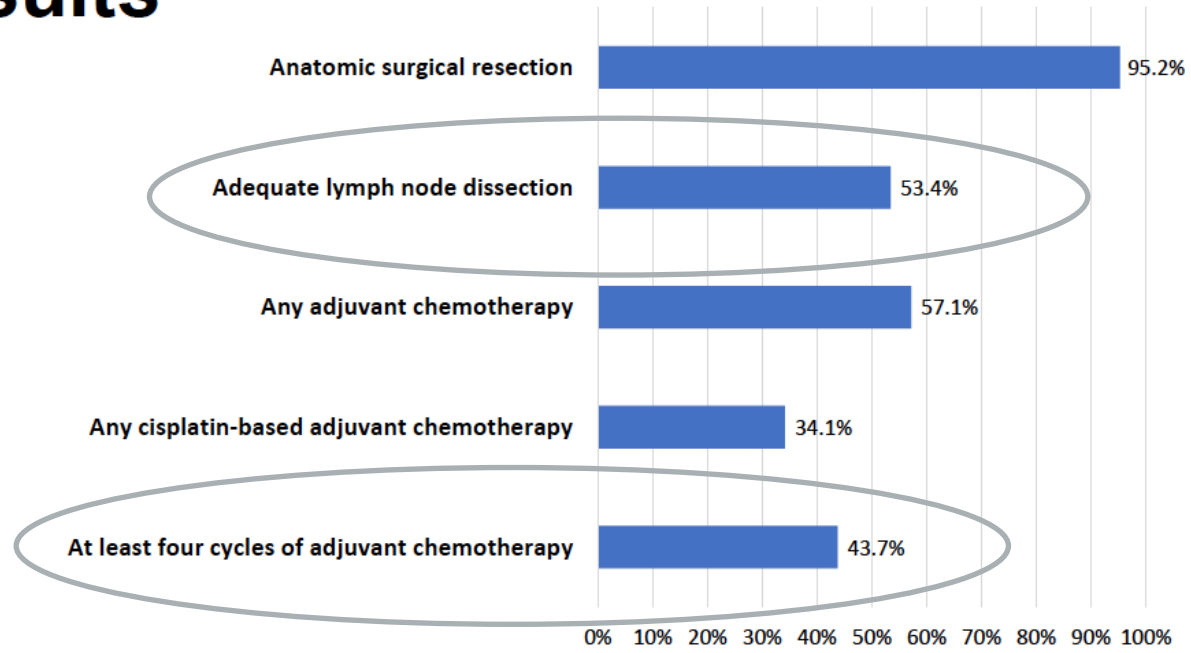
Open: n=28, Median= 1.89, IQR=(1.68, 2.43)
VATS: n=28, Median= 2.07, IQR=(1.63, 2.89)

Low rates of adjuvant uptake: ALCHEMIST

Rates of Guideline-Concordant Surgery and Adjuvant Chemotherapy in the U.S. ALCHEMIST Study (ALLIANCE)

Presenter: Kenneth L. Kehl, MD, MPH
Dana-Farber Cancer Institute
United States

Results



No association between socioeconomic factors and care process outcomes

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Key take away messages

- Neoadjuvant and adjuvant options are expanding
- Patient selection for different treatment strategies will often be made by surgeons
- Neoadjuvant chemo-immunotherapy does not appear to compromise (and may enhance) surgical safety
- Adjuvant therapy won’t delay surgery, but many patients won’t start or complete therapy after surgery
- We still await data on effect of these strategies on overall survival
- Identification of which patients are most likely to benefit and determination of appropriate duration of therapy remain key questions

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