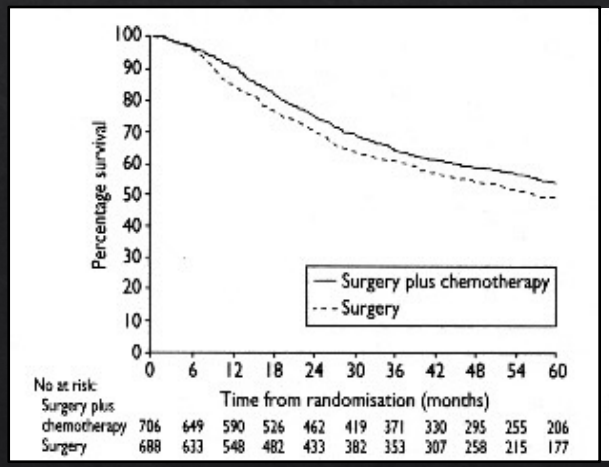
# Advances in early stage and localized NSCLC

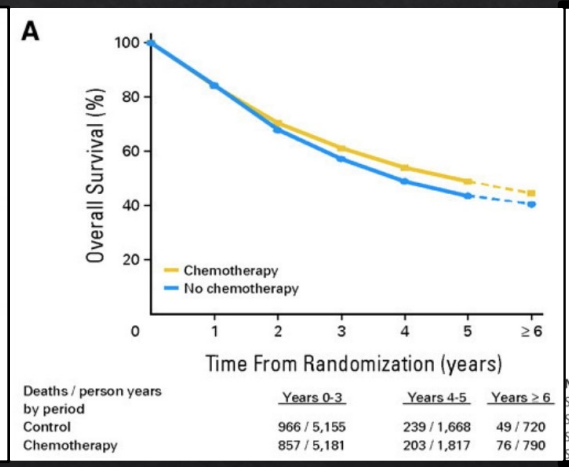
Robert M. Jotte MD PhD
Disease Chair, Lung Committee SCRI
Rocky Mountain Cancer Centers

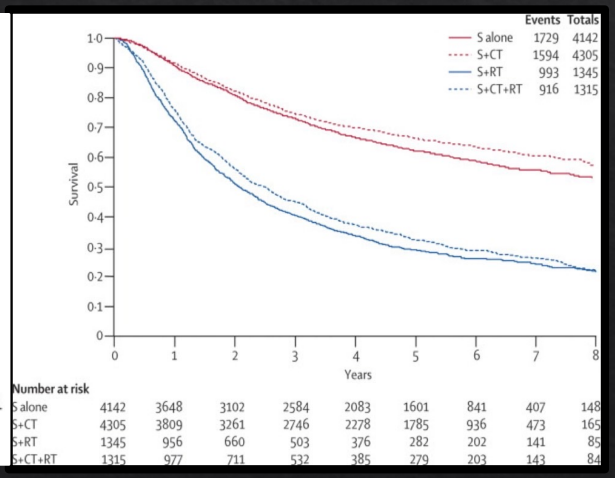
# Adjuvant chemotherapy meta-analyses

| Meta-Analyses | N | 5-year OS benefit | OS HR (95% CI) | p value |
|---|---|---|---|---|
| NSCLCCG 1995 | 1,300 | 5% | 0.87 (0.74-1.02) | 0.08 |
| LACE 2008 | 4,584 | 5.4% | 0.89 (0.82-0.96) | 0.005 |
| NSCLCCG 2010 | 8,447 | 4% | 0.86 (0.81-0.92) | <0.0001 |

Abbreviations: NSCLC, non-small cell lung cancer; OS, overall survival; HR, hazard ratio; CI, confidence interval.



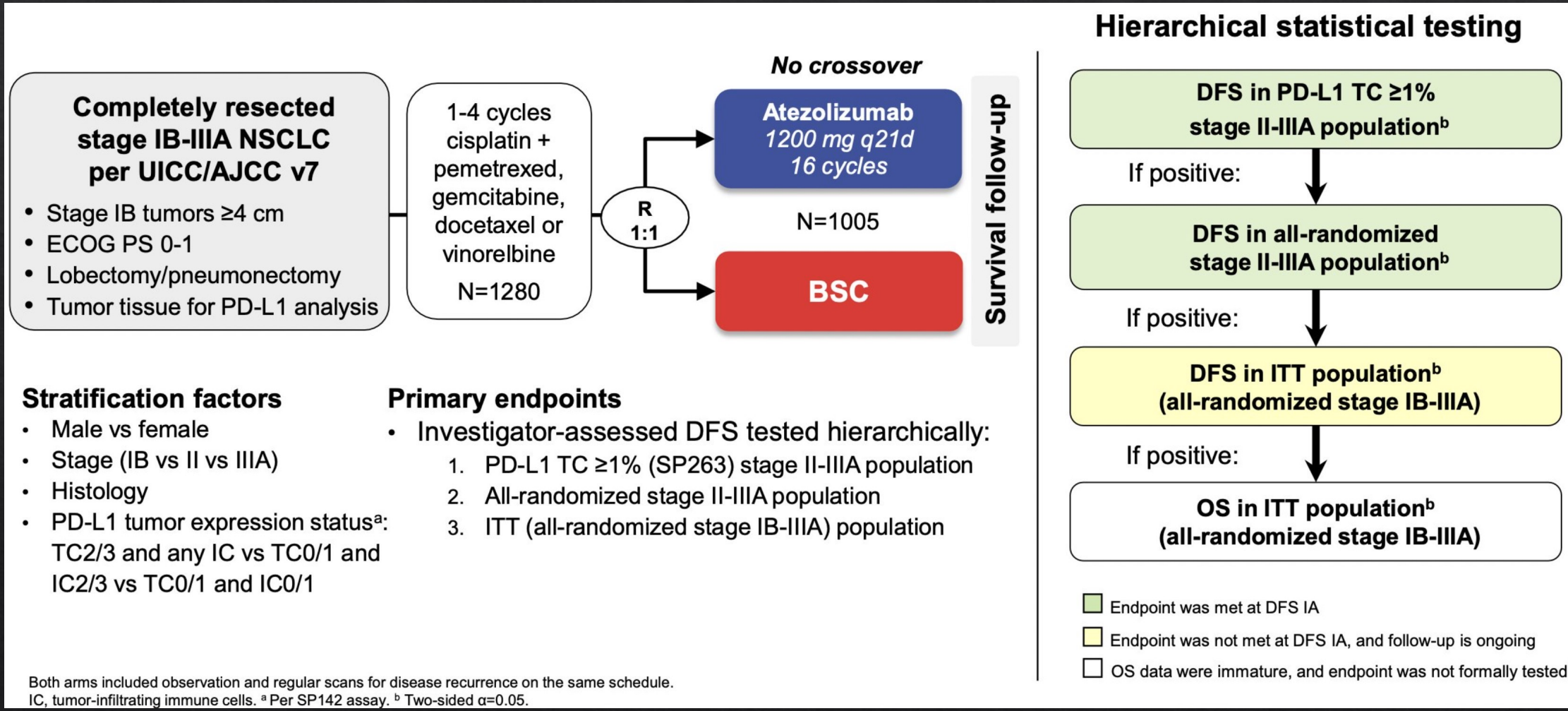


Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomized clinical trials. Br. Med. J. 1995; 311:899.

Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaberative Group. Pignon JP, et al., JCO 2008; 26:3552.

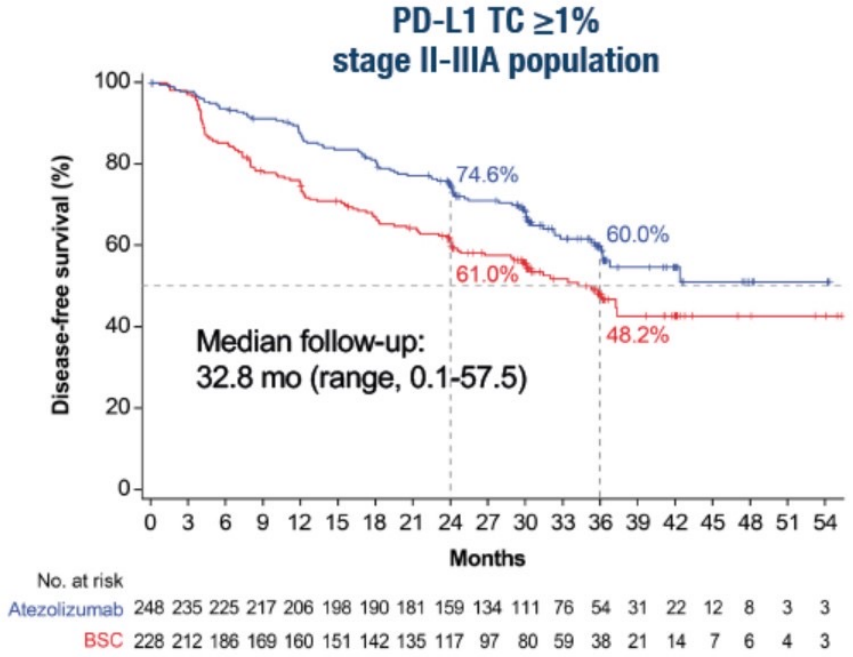
Adjuvant chemotherapy, with or without postoperative radiotherapy, in operable non-small-cell lung cancer: two meta-anlysises of individual patient data. Lancet. 2010; 375:1267.

# IMpower010




Both arms included observation and regular scans for disease recurrence on the same schedule.
IC, tumor-infiltrating immune cells. [a] Per SP142 assay. [b] Two-sided α=0.05.

# IMpower010
# Disease Free Survival (Stage II-III)
# PDL-1 ≥1%




| | 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] | |

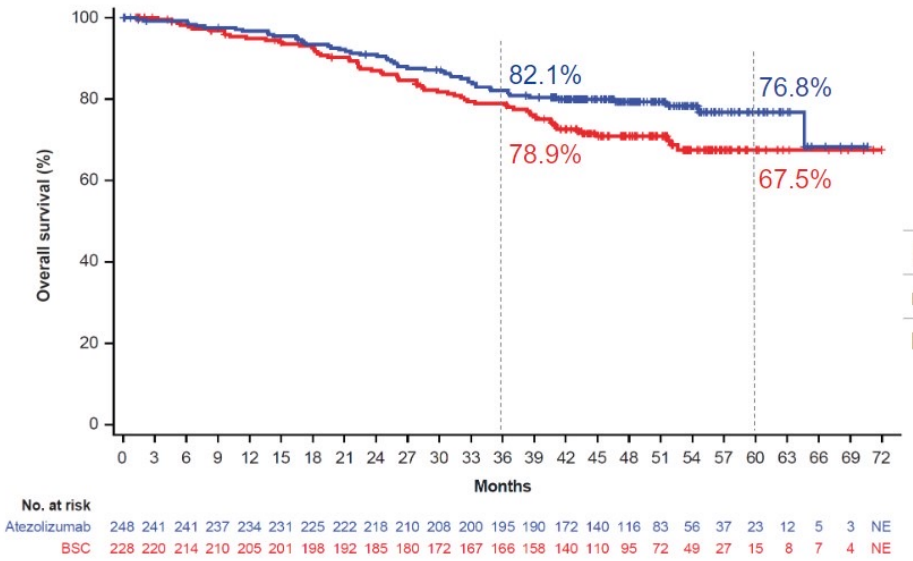
Clinical cutoff: 21 January 2021. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS. [d] The statistical significance boundary for DFS was not crossed. [1.] Wakelee H, et al. J Clin Oncol. 2021;39(suppl 15):8500.

Impower010: Overall survival interim analysis of a phase III study of atezolizumab vs best supportive care in resected NSCLC. Wakelee H et al., 2022 World Conference on Lung Cancer. Abstract PL03.09. Presented Aug. 8, 2022.

# IMpower010
# Overall Survival (Stage II-III)
# PDL-1 ≥1%

## Results of OS IA: PD-L1 TC ≥1%[a] (stage II-IIIA)

*(data cutoff: 18 Apr '22, median follow-up: 46 months)*




| | Atezo (n=248) | BSC (n=228) |
|---|---|---|
| Events, n (%) | 52 (21.0%) | 64 (28.1%) |
| mOS (95% CI), mo | NR | NR |
| HR (95% CI)[b] | 0.71 (0.49, 1.03) | |

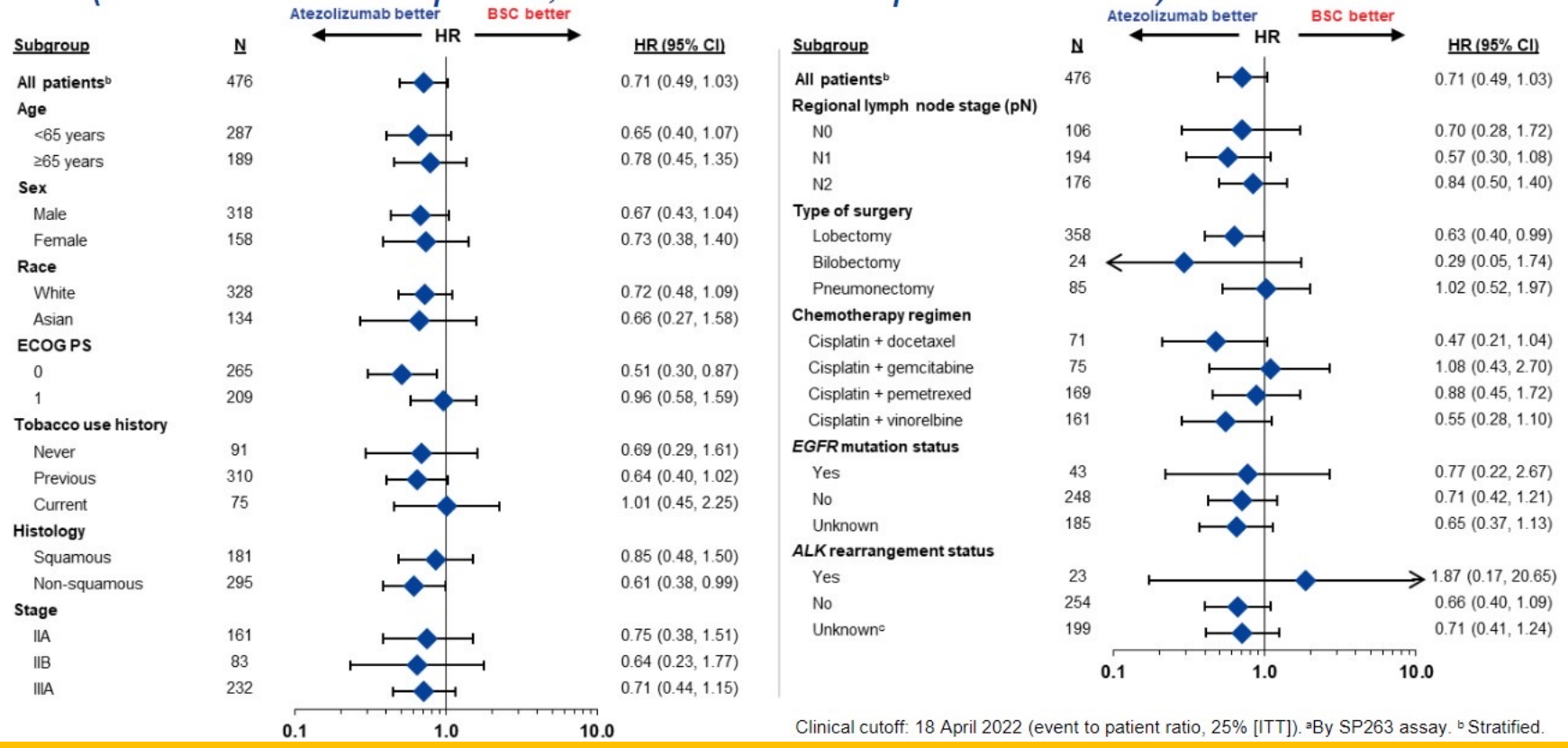
mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

Impower010: Overall survival interim analysis of a phase III study of atezolizumab vs best supportive care in resected NSCLC. Wakelee H et al., 2022 World Conference on Lung Cancer. Abstract PL03.09. Presented Aug. 8, 2022.

# IMpower010
# Subgroup Analysis (Stage II-III)
# PDL-1 ≥1%

## Subgroup analysis of OS in PD-L1 TC ≥1%[a] (stage II-IIIA)

*(data cutoff: 18 Apr '22, median follow-up: 46 months)*




| Subgroup | N | HR (95% CI) |
|---|---|---|
| **All patients[b]** | 476 | 0.71 (0.49, 1.03) |
| **Age** | | |
| <65 years | 287 | 0.65 (0.40, 1.07) |
| ≥65 years | 189 | 0.78 (0.45, 1.35) |
| **Sex** | | |
| Male | 318 | 0.67 (0.43, 1.04) |
| Female | 158 | 0.73 (0.38, 1.40) |
| **Race** | | |
| White | 328 | 0.72 (0.48, 1.09) |
| Asian | 134 | 0.66 (0.27, 1.58) |
| **ECOG PS** | | |
| 0 | 265 | 0.51 (0.30, 0.87) |
| 1 | 209 | 0.96 (0.58, 1.59) |
| **Tobacco use history** | | |
| Never | 91 | 0.69 (0.29, 1.61) |
| Previous | 310 | 0.64 (0.40, 1.02) |
| Current | 75 | 1.01 (0.45, 2.25) |
| **Histology** | | |
| Squamous | 181 | 0.85 (0.48, 1.50) |
| Non-squamous | 295 | 0.61 (0.38, 0.99) |
| **Stage** | | |
| IIA | 161 | 0.75 (0.38, 1.51) |
| IIB | 83 | 0.64 (0.23, 1.77) |
| IIIA | 232 | 0.71 (0.44, 1.15) |




| Subgroup | N | HR (95% CI) |
|---|---|---|
| **All patients[b]** | 476 | 0.71 (0.49, 1.03) |
| **Regional lymph node stage (pN)** | | |
| N0 | 106 | 0.70 (0.28, 1.72) |
| N1 | 194 | 0.57 (0.30, 1.08) |
| N2 | 176 | 0.84 (0.50, 1.40) |
| **Type of surgery** | | |
| Lobectomy | 358 | 0.63 (0.40, 0.99) |
| Bilobectomy | 24 | 0.29 (0.05, 1.74) |
| Pneumonectomy | 85 | 1.02 (0.52, 1.97) |
| **Chemotherapy regimen** | | |
| Cisplatin + docetaxel | 71 | 0.47 (0.21, 1.04) |
| Cisplatin + gemcitabine | 75 | 1.08 (0.43, 2.70) |
| Cisplatin + pemetrexed | 169 | 0.88 (0.45, 1.72) |
| Cisplatin + vinorelbine | 161 | 0.55 (0.28, 1.10) |
| ***EGFR* mutation status** | | |
| Yes | 43 | 0.77 (0.22, 2.67) |
| No | 248 | 0.71 (0.42, 1.21) |
| Unknown | 185 | 0.65 (0.37, 1.13) |
| ***ALK* rearrangement status** | | |
| Yes | 23 | 1.87 (0.17, 20.65) |
| No | 254 | 0.66 (0.40, 1.09) |
| Unknown[c] | 199 | 0.71 (0.41, 1.24) |

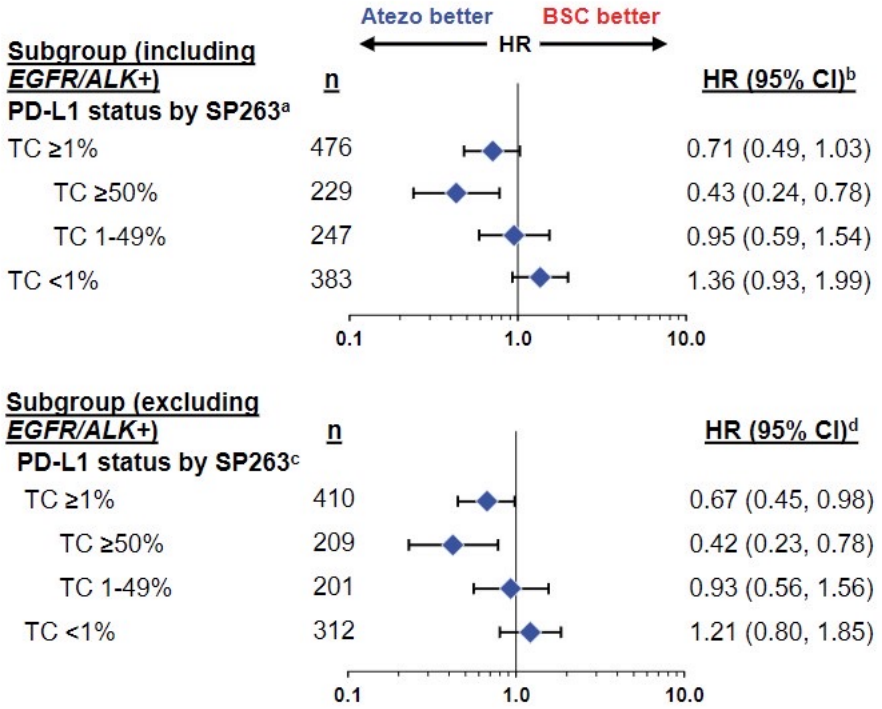
Clinical cutoff: 18 April 2022 (event to patient ratio, 25% [ITT]). [a]By SP263 assay. [b] Stratified.

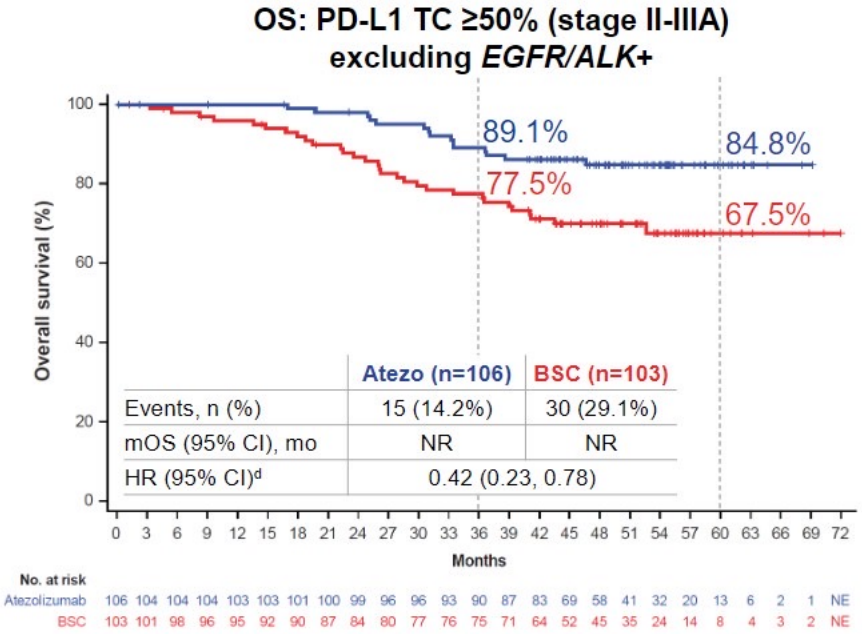
Impower010: Overall survival interim analysis of a phase III study of atezolizumab vs best supportive care in resected NSCLC. Wakelee H et al., 2022 World Conference on Lung Cancer. Abstract PL03.09. Presented Aug. 8, 2022.

# IMpower010 Subgroup Analysis (Stage II-III) by biomarker status

## OS by biomarker status (stage II-IIIA)

*(data cutoff: 18 Apr '22)*




[a] 23 patients had unknown PD-L1 status. [b] Stratified for PD-L1 TC ≥1%; unstratified for all other subgroups. [c] 21 patients had unknown PD-L1 status. [d] Unstratified.

Impower010: Overall survival interim analysis of a phase III study of atezolizumab vs best supportive care in resected NSCLC. Wakelee H et al., 2022 World Conference on Lung Cancer. Abstract PL03.09. Presented Aug. 8, 2022.

# Efficacy of Preoperative Immunotherapy

| Study | Total n= Squam, % | Stage I/II III | Drug # of preoperative cycles | # taken to surgery(%) #R0 | ORR DCR | pCR^ | MPR^ | Biomarker Correlation with MPR |
|---|---|---|---|---|---|---|---|---|
| | | | PD-(L)1 Monotherapy | | | | | |
| Forde NEJM 2018 | 21<br>6 (29%) | 66%<br>33% | Nivo 3 mg/kg<br>x 2 | 21 (100)<br>20 R0 | 10%<br>95% | 10% | 45% | PD-L1: No correlation<br>TMB: Correlation (+) |
| Gao JTO 2021 | 40<br>33 (83%) | 55%<br>45% | Sintilimab 200 mg<br>x 2 | 37 (92.5)<br>36 R0 | 20%<br>90% | 16.2% | 40.5% | PD-L1: Correlation (+)*<br>TMB: NR |
| LCMC3 | 181<br>69 (38%) | 51%<br>49% | Atezo 1200 mg<br>x 2 | 159 (88)<br>145 R0 | 7%**<br>95% | 7% | 21% | PD-L1: No correlation<br>TMB: No correlation |
| NEOSTAR | 23<br>10 (43%) | 78%<br>22% | Nivo 3 mg/kg<br>x 3 | 22 (96)<br>22 R0 | 22%<br>87% | 10% | 19% | PD-L1: Correlation (+)<br>TMB: NR |
| MK3475-223 | 15<br>NR | 100%<br>0% | Pembro 200 mg<br>x 1-2 | 13 (87)<br>NR | 13%<br>NR | 15% | 31%<br>40% (2 doses) | PD-L1: No correlation<br>TMB: NR |
| IFCT-1601 IONESCO | 50<br>21 (42%) | 96%<br>4% | Durva 750 mg<br>x 3 | 43 (93)<br>41 R0 | 9%<br>87% | 7% | 18.6% | PD-L1: NR<br>TMB: NR |
| PRINCEPS | 30<br>NR | 70%<br>30% | Atezo 1200 mg<br>x 1 | 30 (100)<br>29 R0 | 7%<br>100% | 0% | 14% | PD-L1: Correlation (+)<br>TMB: NR |
| | | | Dual Checkpoint Inhibitors | | | | | |
| Reuss JITC 2020 | 9<br>1 (11%) | 33%<br>66% | Nivo 3 mg/kg x3,<br>Ipi 1 mg/kg x 1 | 6 (67%)<br>R0 NR | 11%<br>55% | 33% | 33%<br>(all pCR) | PD-L1: Correlation (+)<br>TMB: No correlation |
| NEOSTAR | 21<br>7 (33%) | 81%<br>19% | Nivo 3 mg/mg x 3<br>Ipi 1 mg/kg x 1 | 17 (81)<br>17 R0 | 19%<br>81% | 38% | 44% | PD-L1: Correlation (+)<br>TMB: NR |

Squam: squamous; ORR: objective response rate; DCR: disease control rate; pCR: pathologic complete response; MPR: major pathologic response; TMB: tumor mutation burden; nivo: nivolumab; atezo: atezolizumab; pembro: pembrolizumab; durva: durvalumab; ipi: ipilimumab; NR: not reported

^Specimens with pCR also included among those with MPR. The denominator is patients undergoing resection. *Correlation in stromal cells only; **Based on data reported for 82 patients

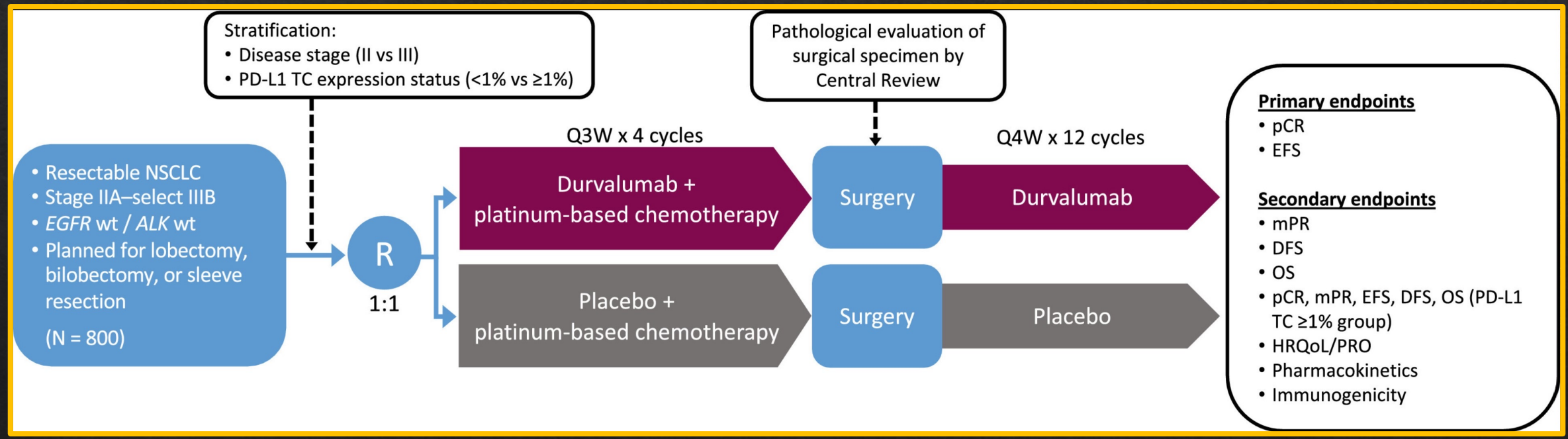
 

# Neoadjuvant Immunotherapy

- CheckMate 816
- AEGEAN
- KEYNOTE 671

# CheckMate 816

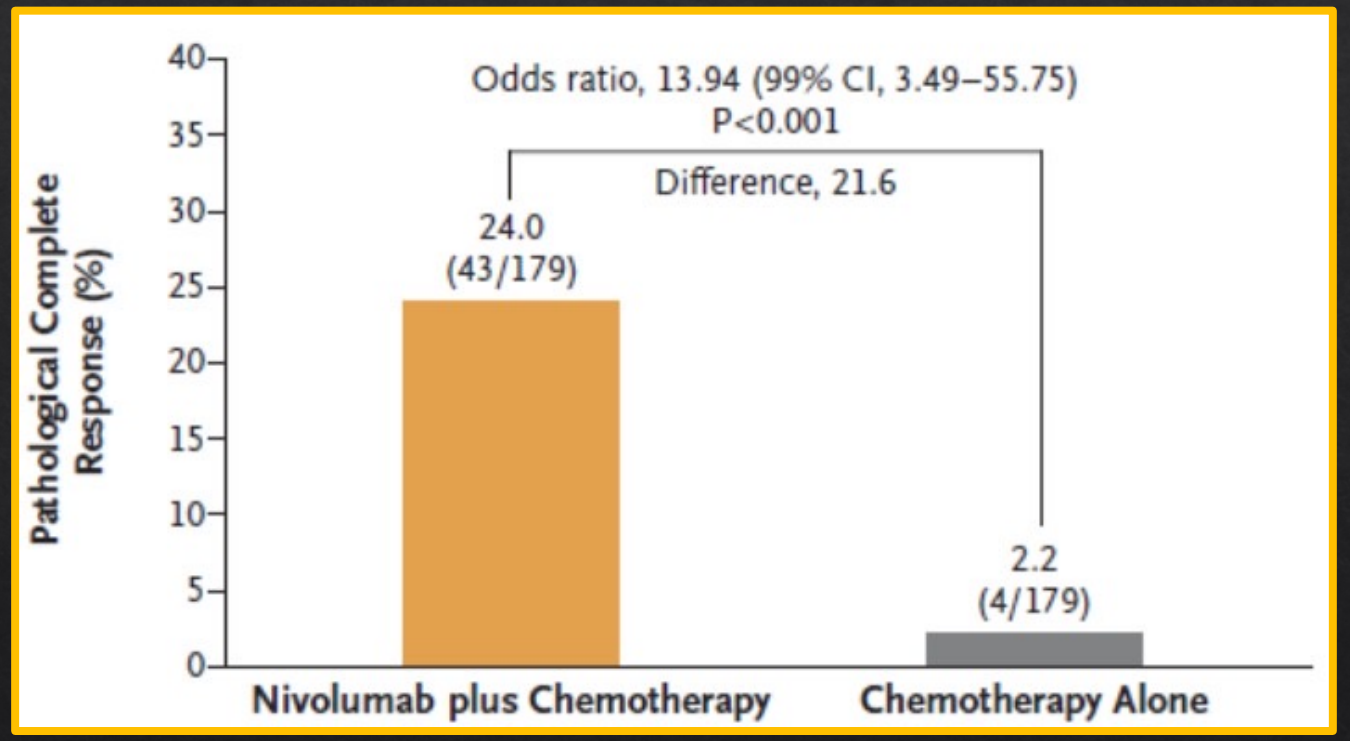
## Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer




Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, et al., 2022. JCO;386:1973.

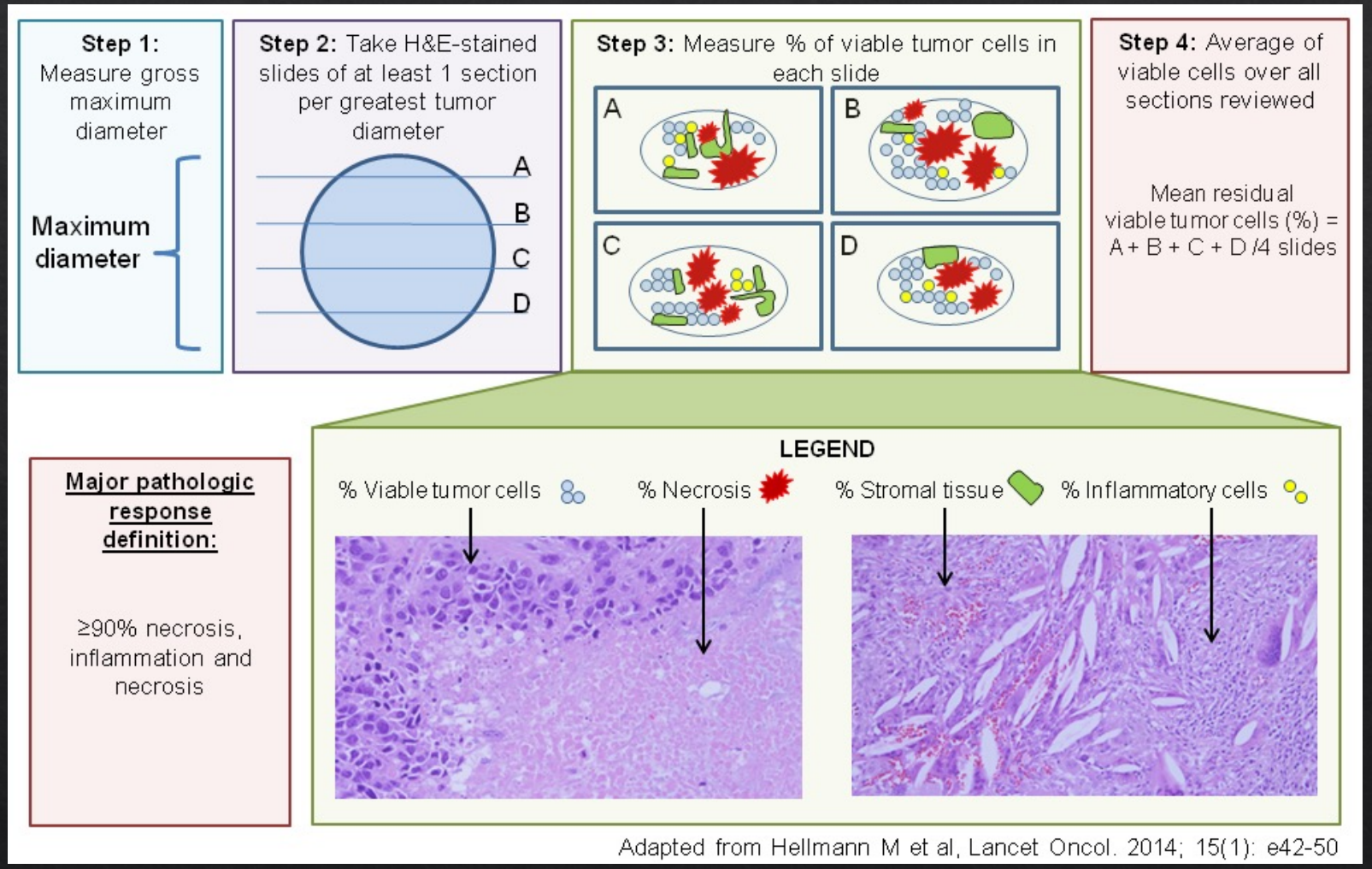
# CheckMate 816

## Pathologic Response Rate




Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, et al., 2022. JCO;386:1973.

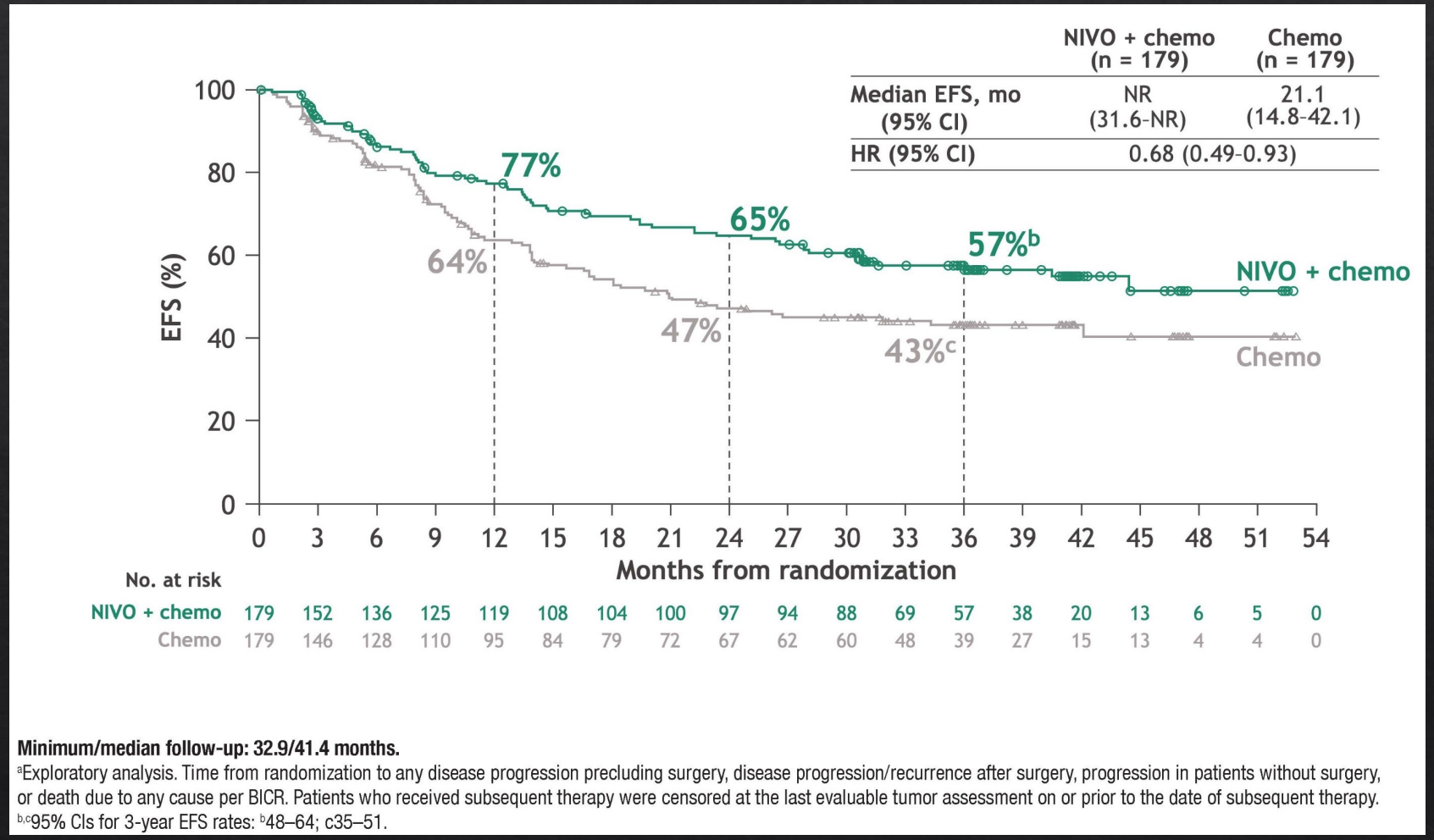
# Pathologic response assessment




Adapted from Hellmann M et al, Lancet Oncol. 2014; 15(1): e42-50

# CheckMate 816

## Event Free Survival




**Minimum/median follow-up: 32.9/41.4 months.**

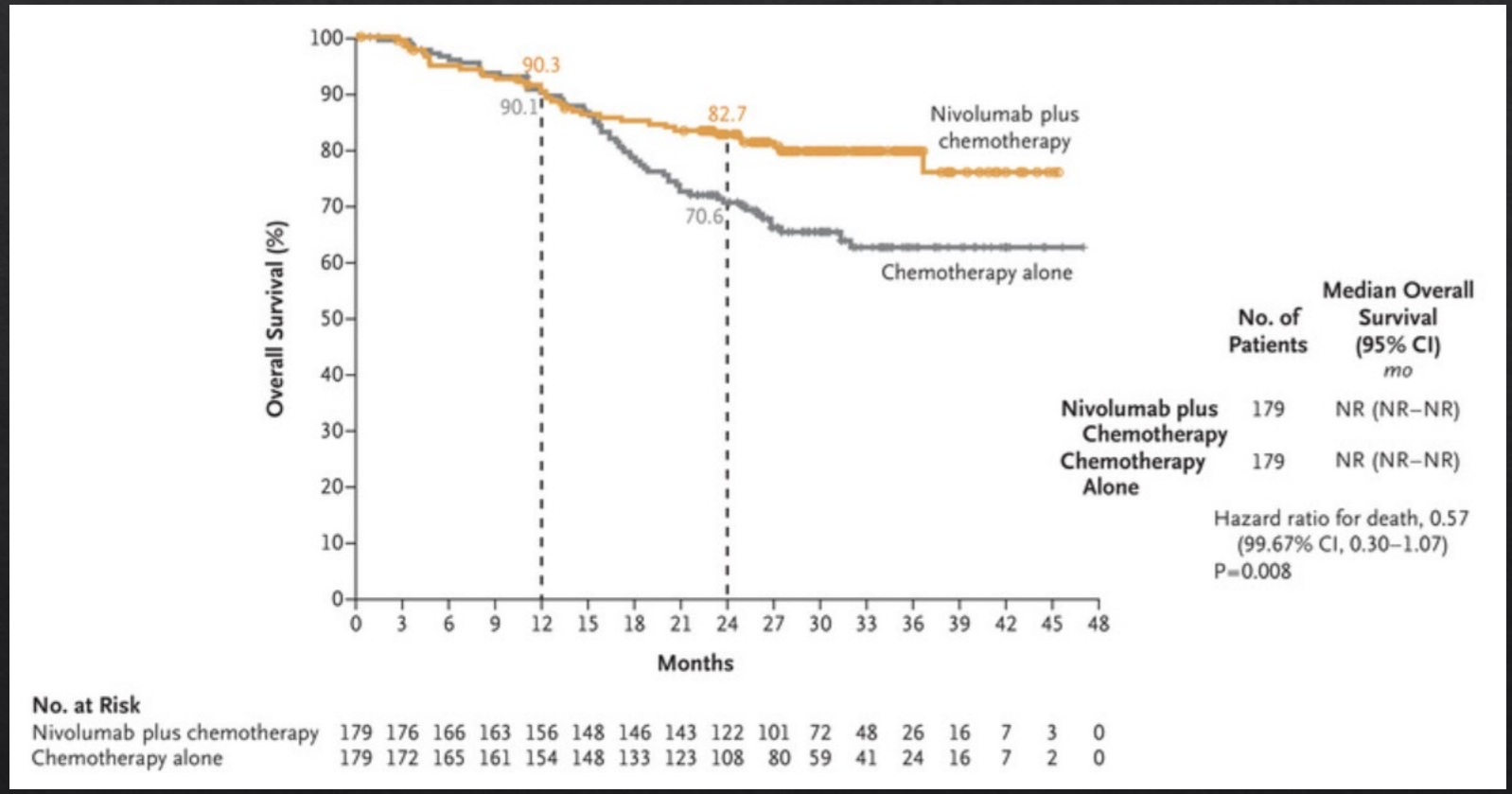
[a]Exploratory analysis. Time from randomization to any disease progression precluding surgery, disease progression/recurrence after surgery, progression in patients without surgery, or death due to any cause per BICR. Patients who received subsequent therapy were censored at the last evaluable tumor assessment on or prior to the date of subsequent therapy.

[b,c]95% CIs for 3-year EFS rates: [b]48–64; c35–51.

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, et al., 2022. JCO;386:1973.

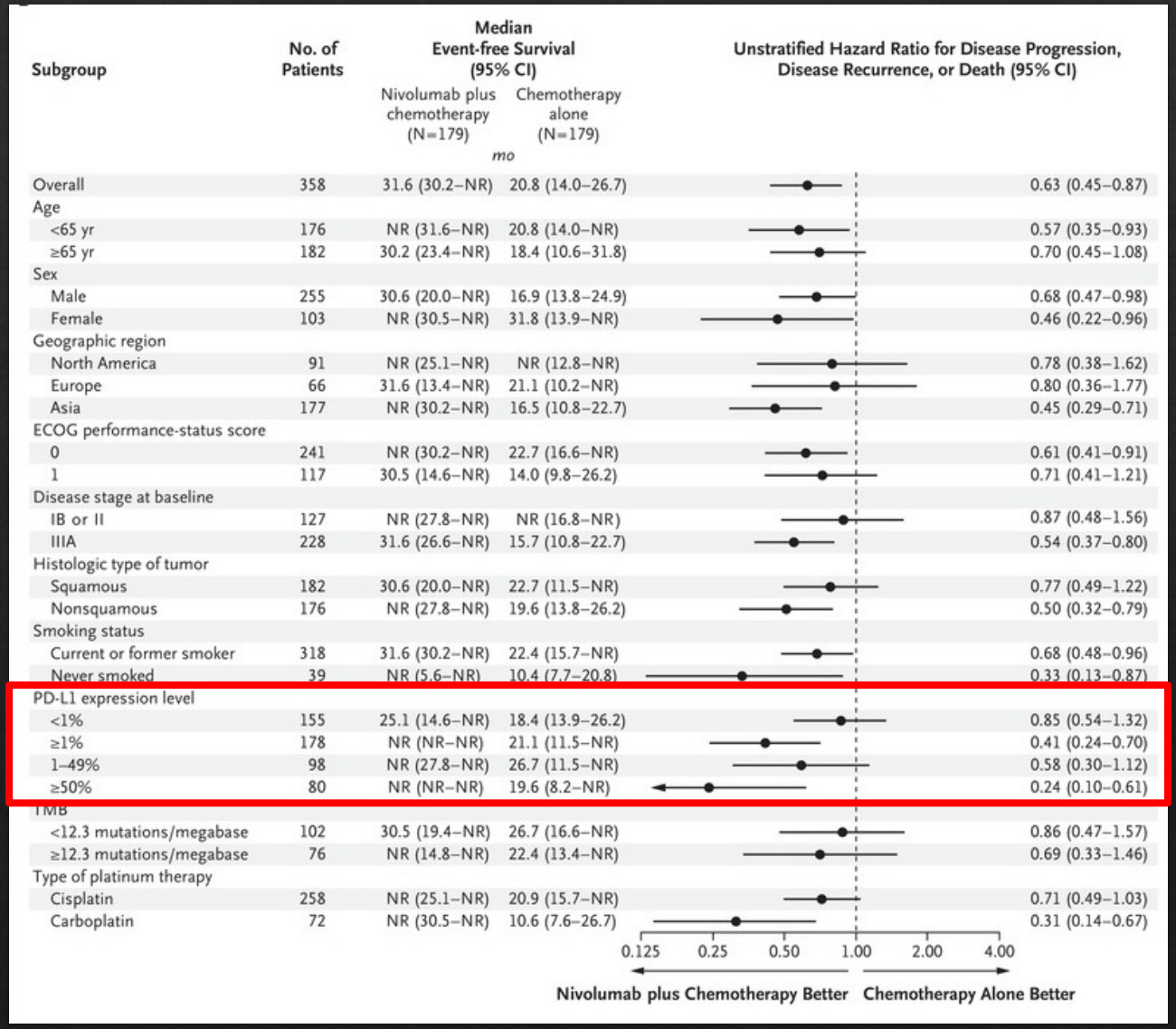
# CheckMate 816

## Overall Survival



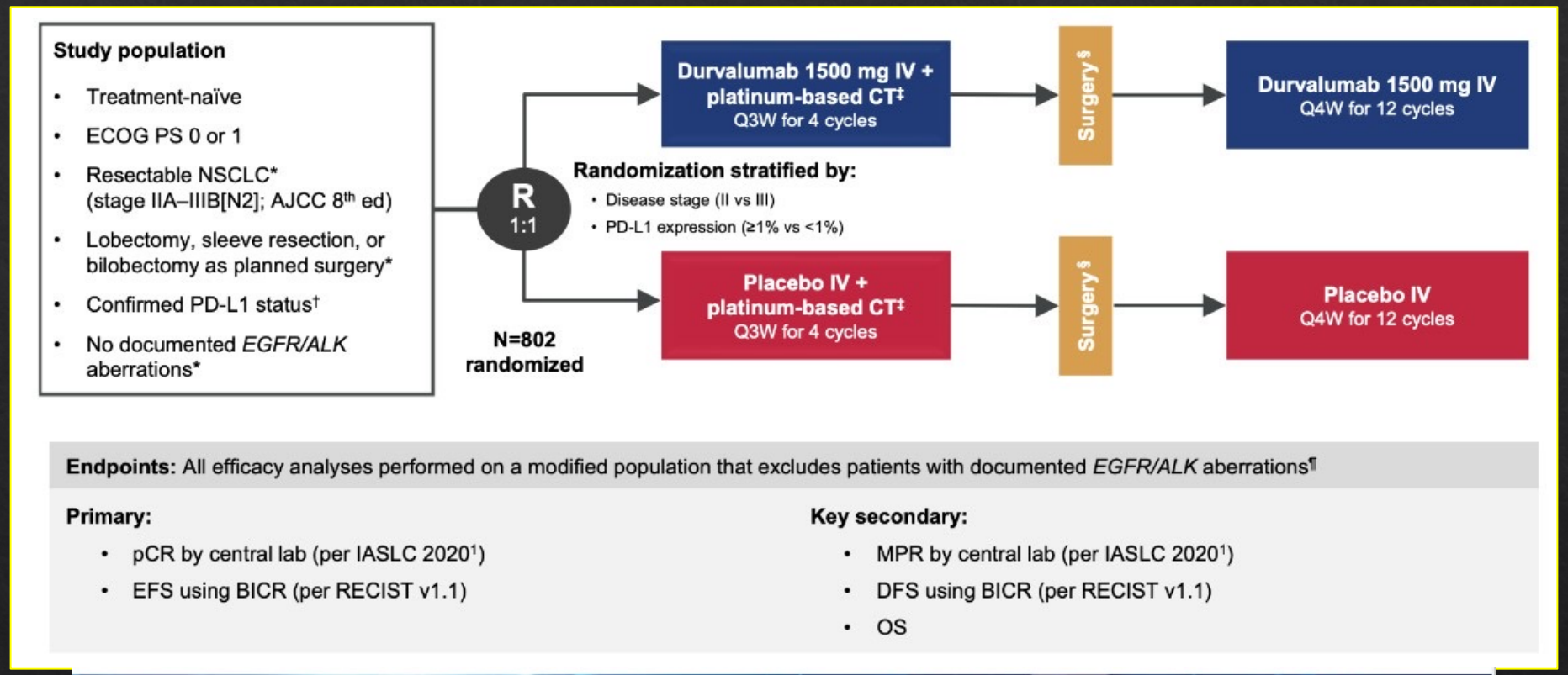

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, et al., 2022. JCO;386:1973.

# Forest plot of EFS in CM816



| Subgroup | No. of Patients | Median Event-free Survival (95% CI) | |
|---|---|---|---|
| | | Nivolumab plus chemotherapy (N=179) | Chemotherapy alone (N=179) |
| | | *mo* | |
| Overall | 358 | 31.6 (30.2–NR) | 20.8 (14.0–26.7) |
| Age | | | |
| <65 yr | 176 | NR (31.6–NR) | 20.8 (14.0–NR) |
| ≥65 yr | 182 | 30.2 (23.4–NR) | 18.4 (10.6–31.8) |
| Sex | | | |
| Male | 255 | 30.6 (20.0–NR) | 16.9 (13.8–24.9) |
| Female | 103 | NR (30.5–NR) | 31.8 (13.9–NR) |
| Geographic region | | | |
| North America | 91 | NR (25.1–NR) | NR (12.8–NR) |
| Europe | 66 | 31.6 (13.4–NR) | 21.1 (10.2–NR) |
| Asia | 177 | NR (30.2–NR) | 16.5 (10.8–22.7) |
| ECOG performance-status score | | | |
| 0 | 241 | NR (30.2–NR) | 22.7 (16.6–NR) |
| 1 | 117 | 30.5 (14.6–NR) | 14.0 (9.8–26.2) |
| Disease stage at baseline | | | |
| IB or II | 127 | NR (27.8–NR) | NR (16.8–NR) |
| IIIA | 228 | 31.6 (26.6–NR) | 15.7 (10.8–22.7) |
| Histologic type of tumor | | | |
| Squamous | 182 | 30.6 (20.0–NR) | 22.7 (11.5–NR) |
| Nonsquamous | 176 | NR (27.8–NR) | 19.6 (13.8–26.2) |
| Smoking status | | | |
| Current or former smoker | 318 | 31.6 (30.2–NR) | 22.4 (15.7–NR) |
| Never smoked | 39 | NR (5.6–NR) | 10.4 (7.7–20.8) |
| PD-L1 expression level | | | |
| <1% | 155 | 25.1 (14.6–NR) | 18.4 (13.9–26.2) |
| ≥1% | 178 | NR (NR–NR) | 21.1 (11.5–NR) |
| 1–49% | 98 | NR (27.8–NR) | 26.7 (11.5–NR) |
| ≥50% | 80 | NR (NR–NR) | 19.6 (8.2–NR) |
| TMB | | | |
| <12.3 mutations/megabase | 102 | 30.5 (19.4–NR) | 26.7 (16.6–NR) |
| ≥12.3 mutations/megabase | 76 | NR (14.8–NR) | 22.4 (13.4–NR) |
| Type of platinum therapy | | | |
| Cisplatin | 258 | NR (25.1–NR) | 20.9 (15.7–NR) |
| Carboplatin | 72 | NR (30.5–NR) | 10.6 (7.6–26.7) |

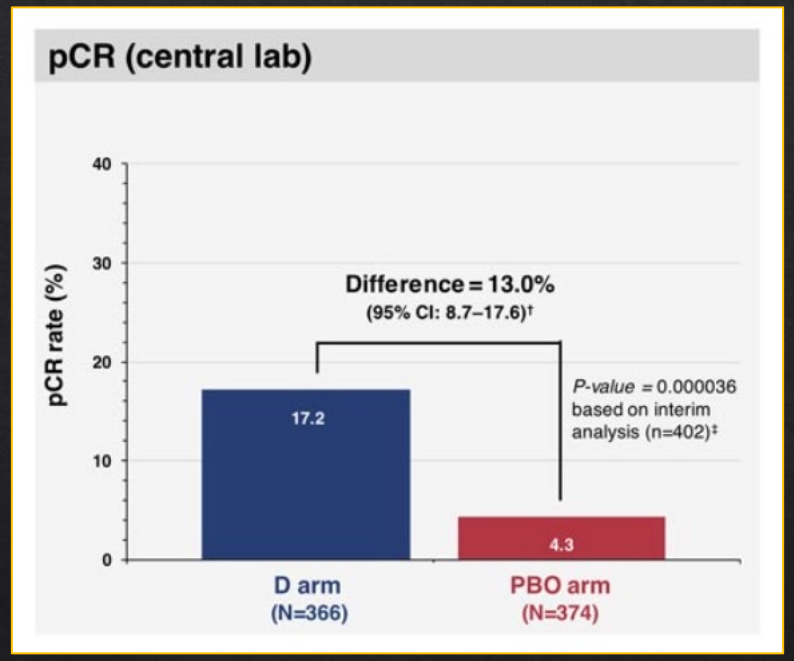
# AEGEAN

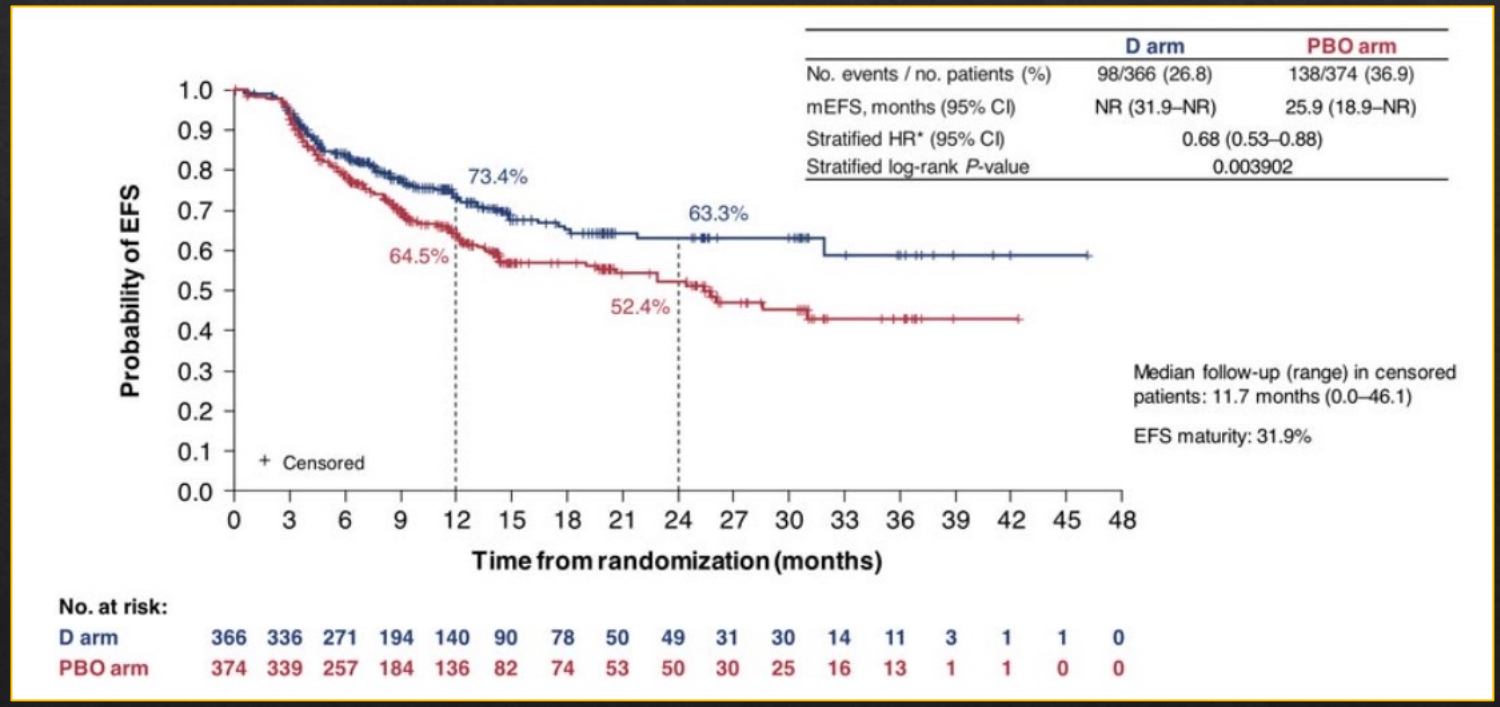




Heymach JV. Abstract CT005:AEGEAN: A phase 3 trial of neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in patients with resectable NSCLC. Can Res 83:15 Apr 2023.

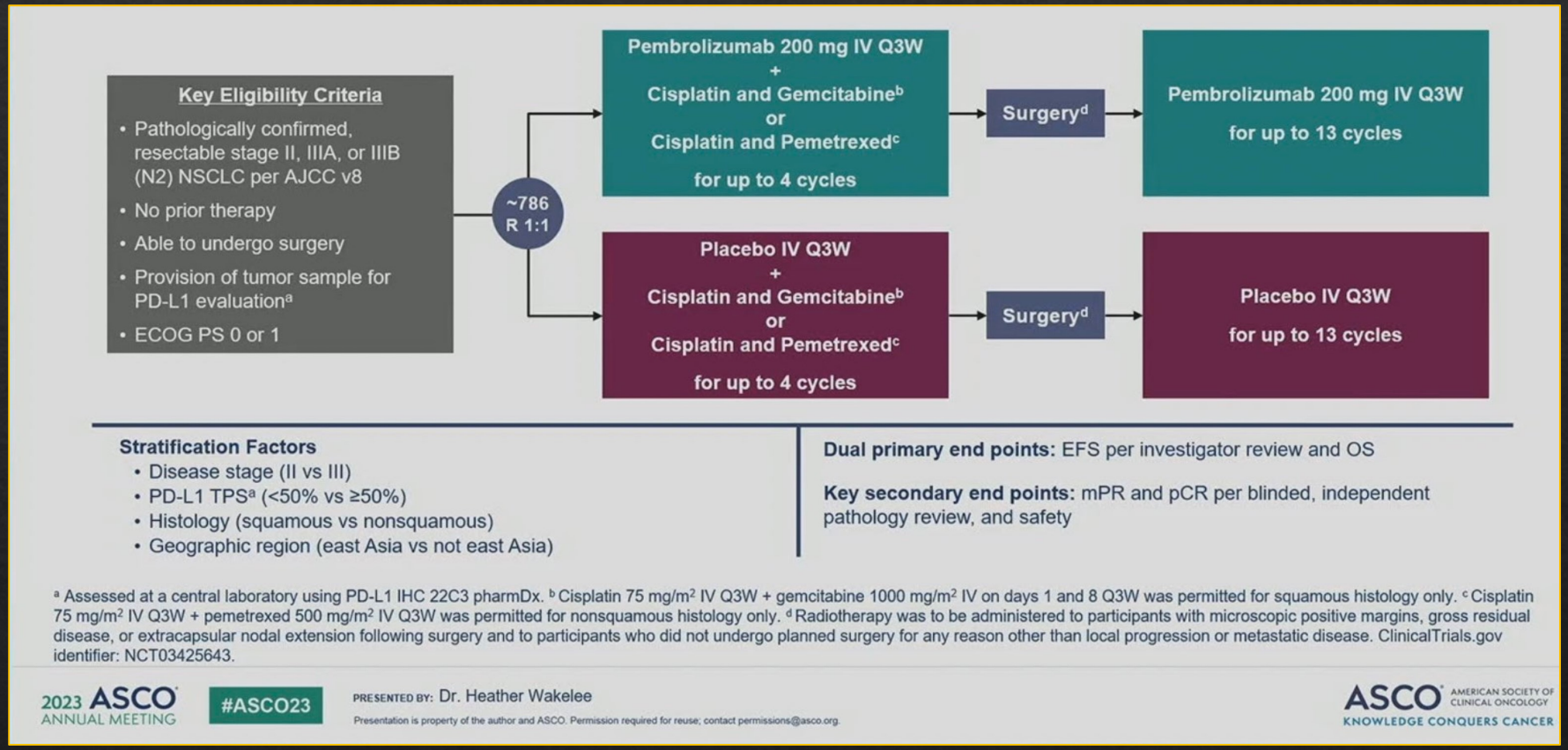
# AEGEAN
# pathologic CR rate and EFS




Heymach JV. Abstract CT005:AEGEAN: A phase 3 trial of neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in patients with resectable NSCLC. Can Res 83:15 Apr 2023.

# KEYNOTE 671


Key Eligibility Criteria
• Pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8
• No prior therapy
• Able to undergo surgery
• Provision of tumor sample for PD-L1 evaluation[a]
• ECOG PS 0 or 1
~786
R 1:1
Pembrolizumab 200 mg IV Q3W
+
Cisplatin and Gemcitabine[b]
or
Cisplatin and Pemetrexed[c]
for up to 4 cycles
Surgery[d]
Pembrolizumab 200 mg IV Q3W
for up to 13 cycles
Placebo IV Q3W
+
Cisplatin and Gemcitabine[b]
or
Cisplatin and Pemetrexed[c]
for up to 4 cycles
Surgery[d]
Placebo IV Q3W
for up to 13 cycles
Stratification Factors
• Disease stage (II vs III)
• PD-L1 TPS[a] (<50% vs ≥50%)
• Histology (squamous vs nonsquamous)
• Geographic region (east Asia vs not east Asia)
Dual primary end points: EFS per investigator review and OS
Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety
[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m² IV Q3W + gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m² IV Q3W + pemetrexed 500 mg/m² IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.
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PRESENTED BY: Dr. Heather Wakelee
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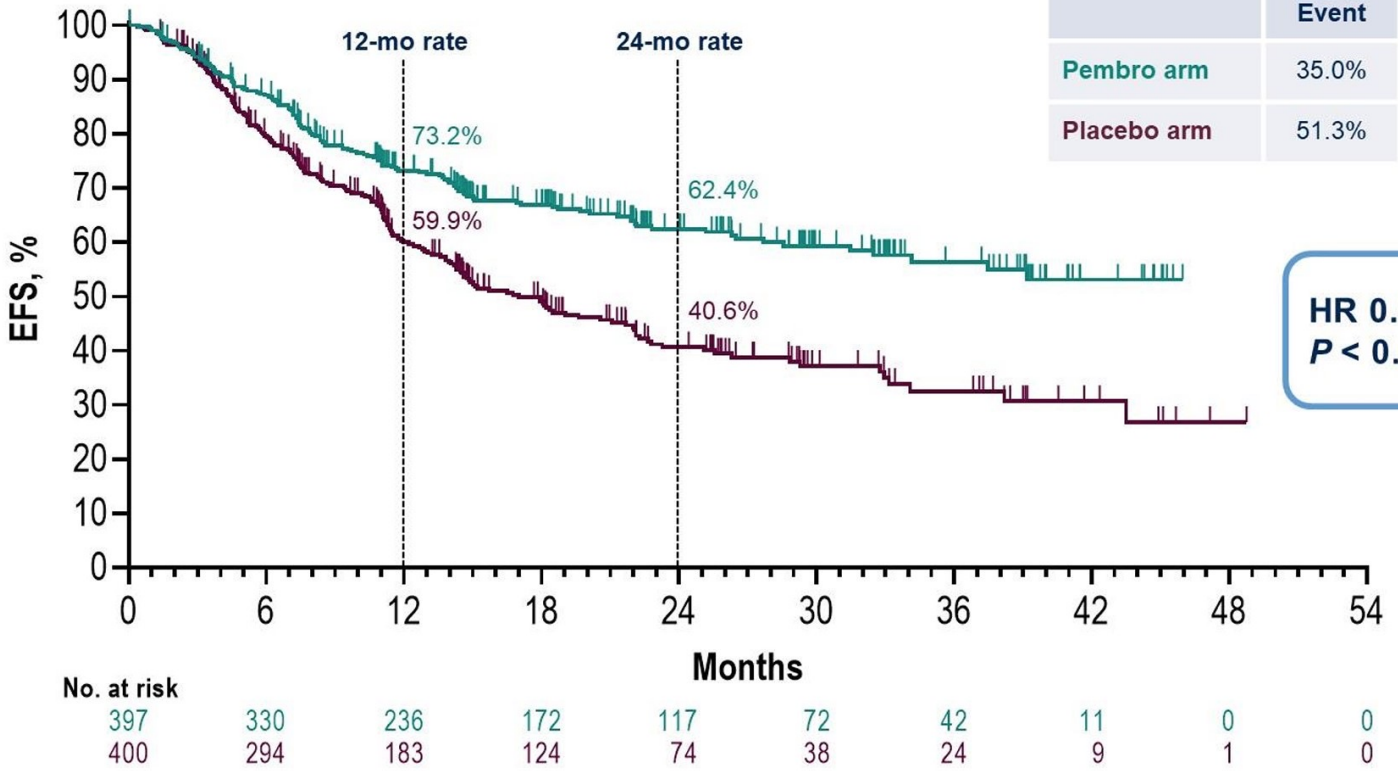
KNOWLEDGE CONQUERS CANCER

# KEYNOTE 671

## Event-Free Survival




| | Pts w/ Event | Median (95% CI), mo |
|---|---|---|
| Pembro arm | 35.0% | NR (34.1-NR) |
| Placebo arm | 51.3% | 17.0 (14.3-22.0) |

**HR 0.58 (95% CI, 0.46-0.72)**
***P* < 0.00001**

EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause.
Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

# Summary of Immunotherapy Options in Early Stage NSCLC

**CheckMate 816**
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Nivolumab
↓
Surgery

78% OS at 36 mos
57% EFS at 36 mos

**AEGEAN***
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Durvalumab
↓
Surgery

73% EFS at 12 mos
63% EFS at 24 mos

**KEYNOTE 671***
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Pembrolizumab
↓
Surgery

73% EFS at 12 mos
62% EFS at 24 mos

**IMpower010**
Resectable Stage II-III

Surgery
↓
Adjuvant Chemotherapy
↓
Atezolizumab x 12 mos
(PDL-1 ≥1%)

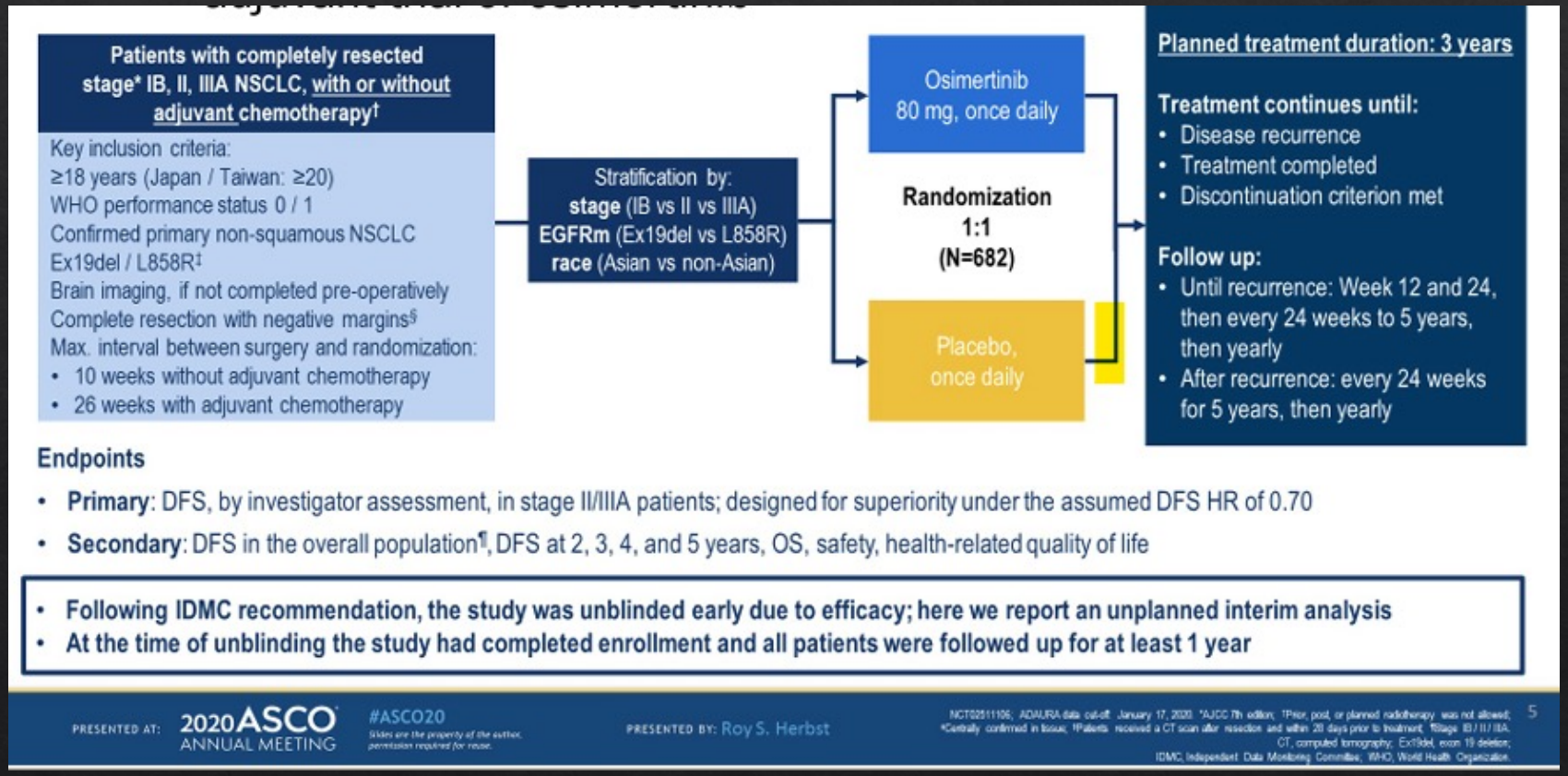
82% OS at 36 mos
75% DFS at 36 mos

# Stage I NSCLC: SBRT + IO Combinations

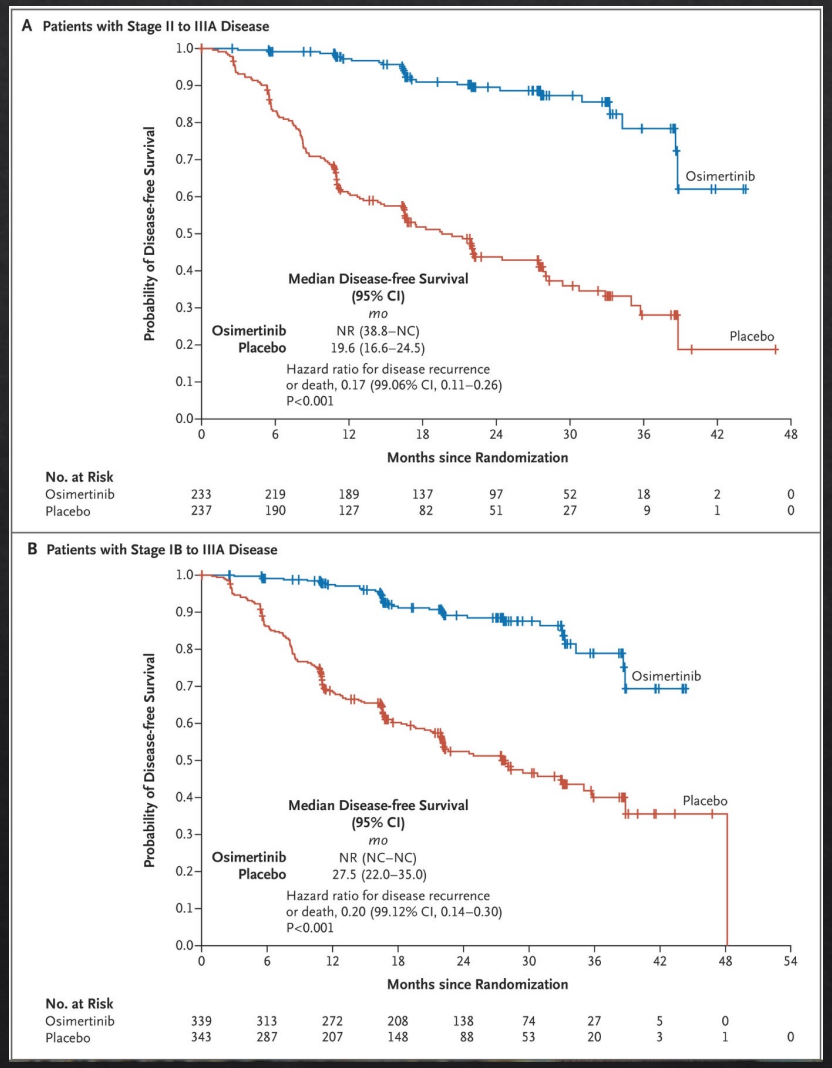
| Study Name | Phase | Arm I SBRT | Arm II SBRT + IO | Placebo | Primary Endpoints |
|---|---|---|---|---|---|
| **PACIFIC-4**<br><br>N = 706 | III | Standard of care 3, 4, 5 or 8 fraction regimens | SBRT followed by Durvalumab 1500 mg Q 4 w x 24 months | Yes | PFS |
| **SWOG/NRG S1914**<br><br>N = 480 | III | Standard of care 3-5 fractions | Atezolizumab x Q 3 w x 2 → SBRT + Atezolizumab → Atezolizumab (8 cycles total) | No | EFS, OS |
| **KEYNOTE-867**<br><br>N = 530 | III | Standard of care 3 – 5 fractions | SBRT followed by Pembrolizumab 200 mg Q 3 week x 12 months | Yes | OS |

# Targeted Adjuvant/Neoadjuvant Therapy

# ADAURA Trial



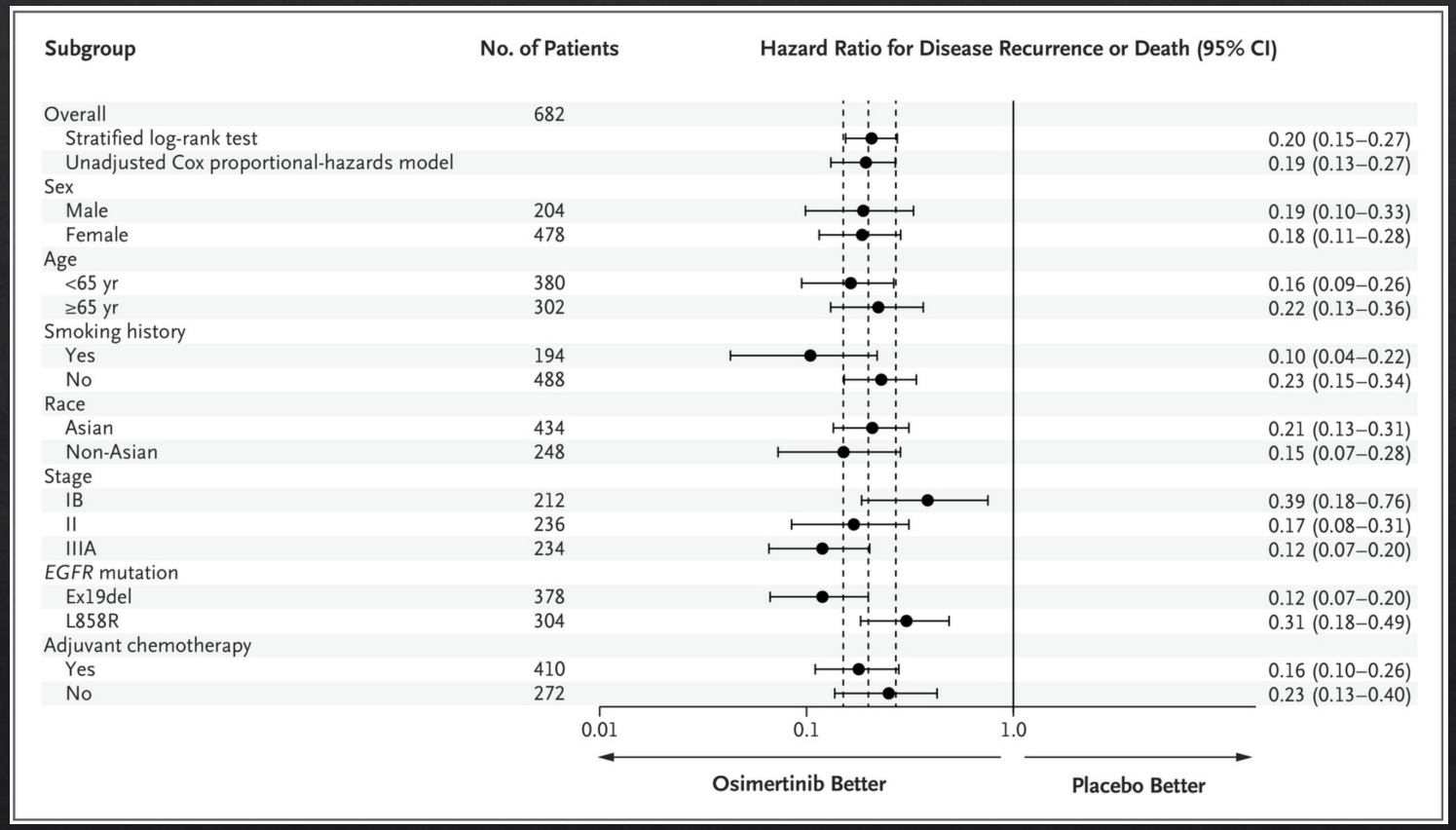
# ADAURA Adjuvant Osi vs Placebo 4 Year DFS F/U




About 1/3 of patients received no adjuvant chemo

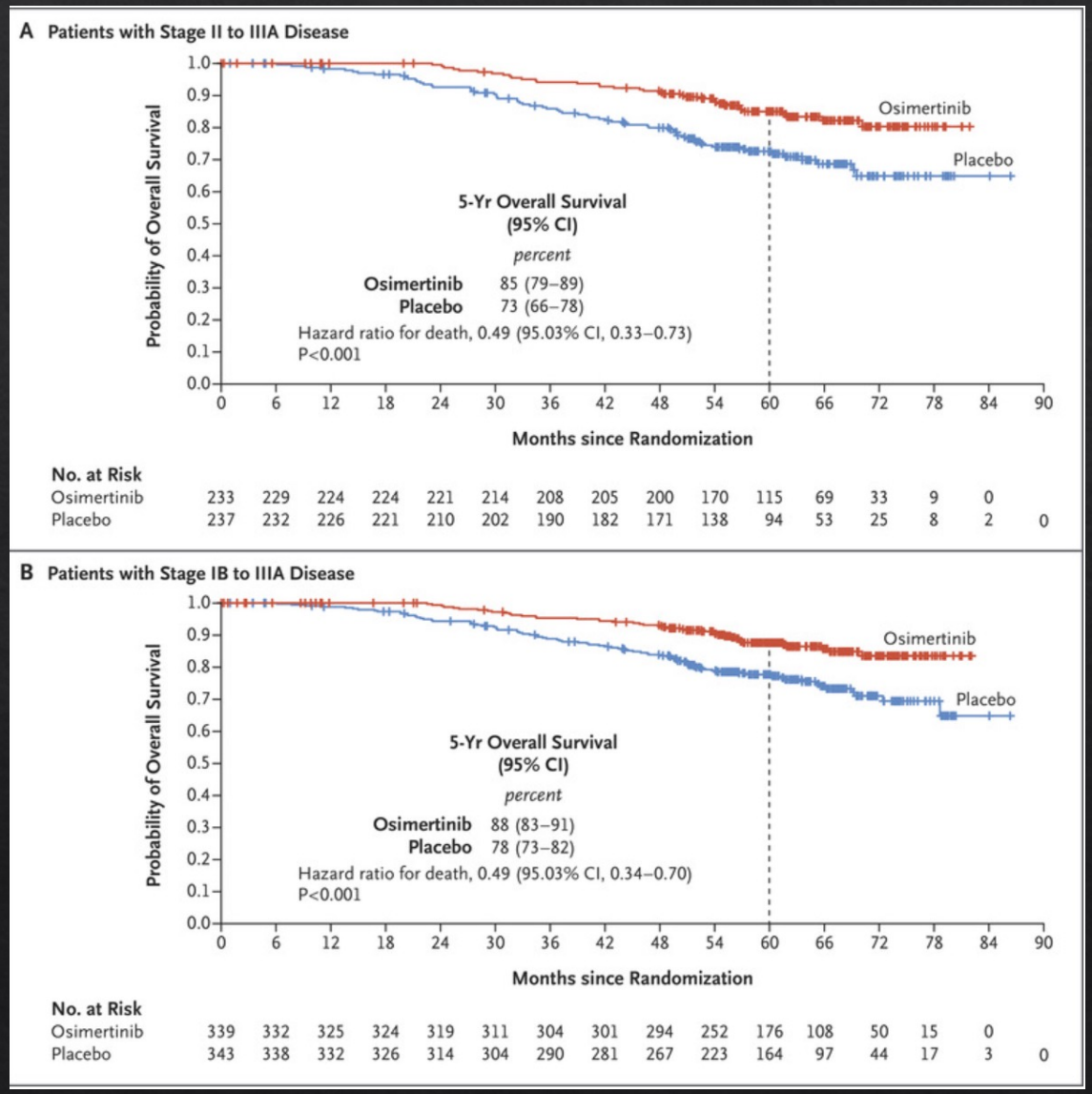
Yi-Long, W et al., NEJM. 2020; 383:1711.

# ADAURA FOREST Plot of Risk factors




Yi-Long, W et al., NEJM. 2020; 383:1711.

# ADAURA Adjuvant Osi vs Placebo 5 Year OS F/U




Tsuboi M, et al., 2023. NEJM;389:137.

# Ongoing adjuvant TKI trials in *ALK+*, *RET+*

## ALINA (NCT03456076), ph III

- Resected stage IB (≥ 4 cm)–IIIA*
- *ALK+* NSCLC
- ECOG PS 0-1

N=257

R 1:1

- Alectinib 600 mg BID, 2 years
- Platinum-based CT, 4 cycles

Stratify by:
- Stage IB vs. II vs. IIIA
- Race (Asian vs. non-Asian)

**Primary Endpoint:** DFS

*IIIA N2 post-operative RT not allowed

## ALCHEMIST (NCT02194738), ph III

ALCHEMIST-screening

| Eligibility | Consent | Specimens | Follow-up |
|---|---|---|---|
| Resected or resectable non-squamous NSCLC, stage IB (≥4cm)–IIIA | Preoperative, during adjuvant therapy, or after | Tumor for EGFR and ALK genotyping, blood, and tissue to NCI | Patients not going into treatment trials are followed every 6 months for 5 years |

- EGFR-mutant → ALCHEMIST-EGFR: Phase III trial of erlotinib vs placebo x 2 years (n=410) — Closed
- ALK-rearranged → ALCHEMIST-ALK: Phase III trial of crizotinib vs placebo x 2 years (n=360)

**Primary Endpoint:** OS

## Heberi University (NCT05241028), ph II

- Resected stage IB (≥ 4 cm)–IIIA
- *ALK+* NSCLC
- ECOG PS 0-1

N=80

→ Ensartinib 225 mg PO, 3 years

**Primary Endpoint:** 3-year DFS

## Sichuan University (NCT05186506), ph II

- Resected stage II-IIIA
- *ALK+* NSCLC
- ECOG PS 0-1

N=152

R 1:1

- Ensartinib 225 mg, PO 2 years
- Platinum-based CT 4 cycles

**Primary Endpoint:** DFS

## LIBRETTO-432 (NCT04819100), ph III

- *RET* fusion-positive NSCLC (Stage IB/IIIA)
- Received locoregional definitive therapy (surgery or radiotherapy)
- No evidence of disease recurrence following definitive therapy as well as adjuvant therapy*

Stratification factors
- Disease stage (Stage IB/IIIA)
- Prior definitive therapy (surgery, radiotherapy)

Randomize (1:1) N (Overall) = 170 — Double-Blind Trial

- ARM A: Selpercatinib (Participants ≥ 50 kg: 160 mg BID; Participants < 50 kg: 120 mg BID)
- ARM B: Placebo (Matching dosage units to Arm A BID)

Recurrence → Survival Follow-Up

Crossover*

*Crossover to selpercatinib allowed ONLY at disease recurrence or progression (per RECIST v1.1 and/or histopathological confirmation)

**Primary Endpoint:** EFS

*Participants must have undergone the available anti-cancer therapy (including chemotherapy or durvalumab) or not be suitable for it, based on the investigator's discretion

# Ongoing clinical trials with *NEOADJ* TKI

## NAUTIKA1 (NCT04302025)

Patients will receive 8 weeks (2 cycles) of neoadjuvant therapy

**Key eligibility criteria**
- Resectable Stage IIA, IIB, IIIA or select IIIB (T3N2) NSCLC
- *ALK+*, *ROS1+*, *NTRK+*, *RET+* or *BRAF V600* mut+
- ECOG PS 0–1
- No prior therapy for lung cancer within 2 years

- *ALK+* cohort: Alectinib 600mg BID (N=~20)
- *ROS1+* cohort: Entrectinib 600mg QD (N=~20)
- *NTRK+* cohort: Entrectinib 600mg QD (N=~20)
- *BRAF* cohort: Vemurafenib 960mg BID + cobimetinib 60mg QD* (N=~20)
- *RET+* cohort: Pralsetinib 400mg QD (N=~20)

→ Surgery

Surveillance period (3 years)
- Platinum-based chemotherapy* (up to 4 cycles)
- Cohort-specific adjuvant TKI† (up to 2 years)
- Surveillance only

→ Survival follow-up (up to 2 years)

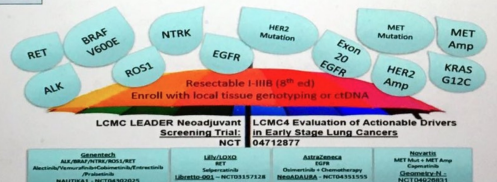
**End Point: MPR**

No surgery performed → Survival follow-up (up to 5 years)

## LCMC4 (NCT04712877)

**LCMC4 Screening Study**
1000 Patients
Stages I-III
Lung Cancers (8th Ed)
Operable
Resectable

**Matched Targeted Therapy Trials**
Industry sponsored




Complete and major pathologic response assessment
Percent viable cells in resection specimen
Correlates in persister cells
Adjuvant therapy – per protocol or investigator's choice

## ALNEO (NCT05015010)

- III (Any T N2 or T4 N0-1)
- *ALK* positive
- PET and Brain MRI
- N=33

→ Alectinib 600 mg PO 8 weeks → Surgery → Alectinib 600 mg PO 96 weeks

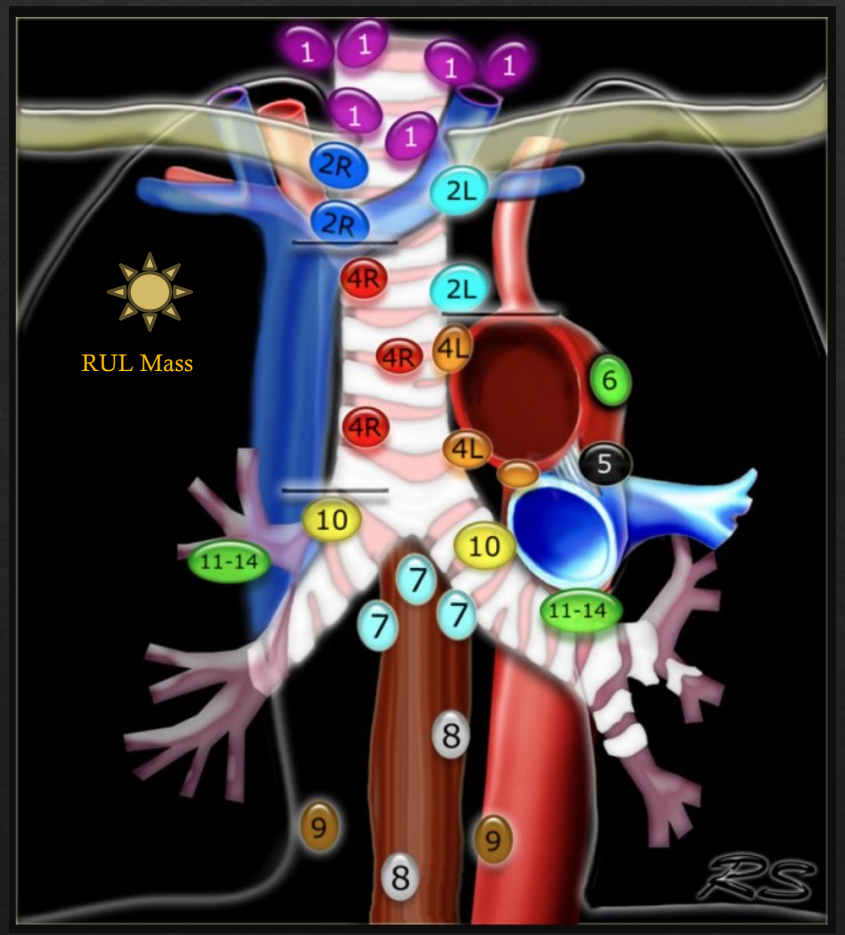
**End Point: MPR**

Lee –WCLC 2021 * Chaft – ESMO 2021

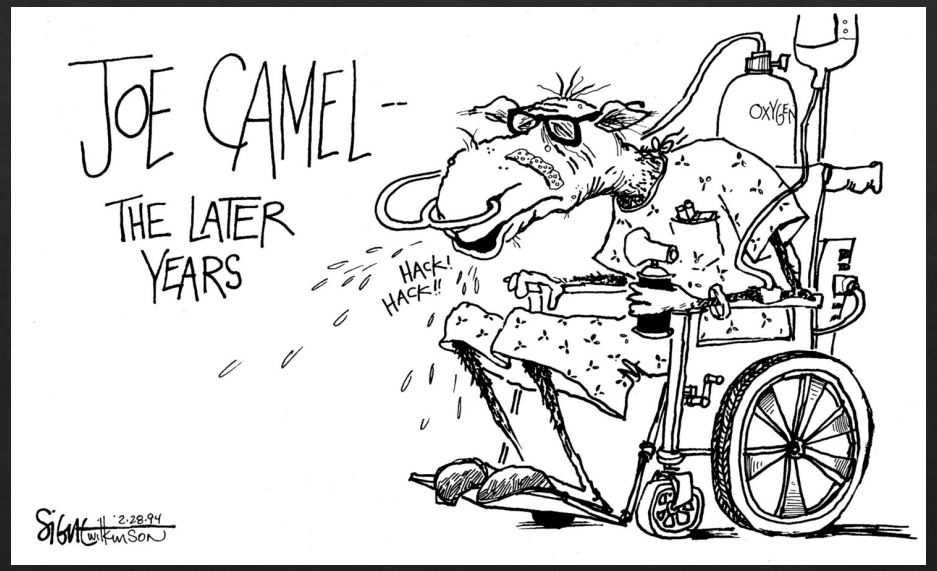
# Major Remaining Questions: Neoadjuvant IO+CT & TKI Rx

- How many pre-op cycles? 2 vs 3
- Need for post-op adjuvant IO?
  - Does pCR matter?
  - Does ctDNA matter?
- Stage IB included?
- Baseline MRIs
- Does PD-L1 status matter?
- Should patients with genetic alterations receive neoadjuvant TKI (duration?) or CT/IO?

# Unresectable Stage III

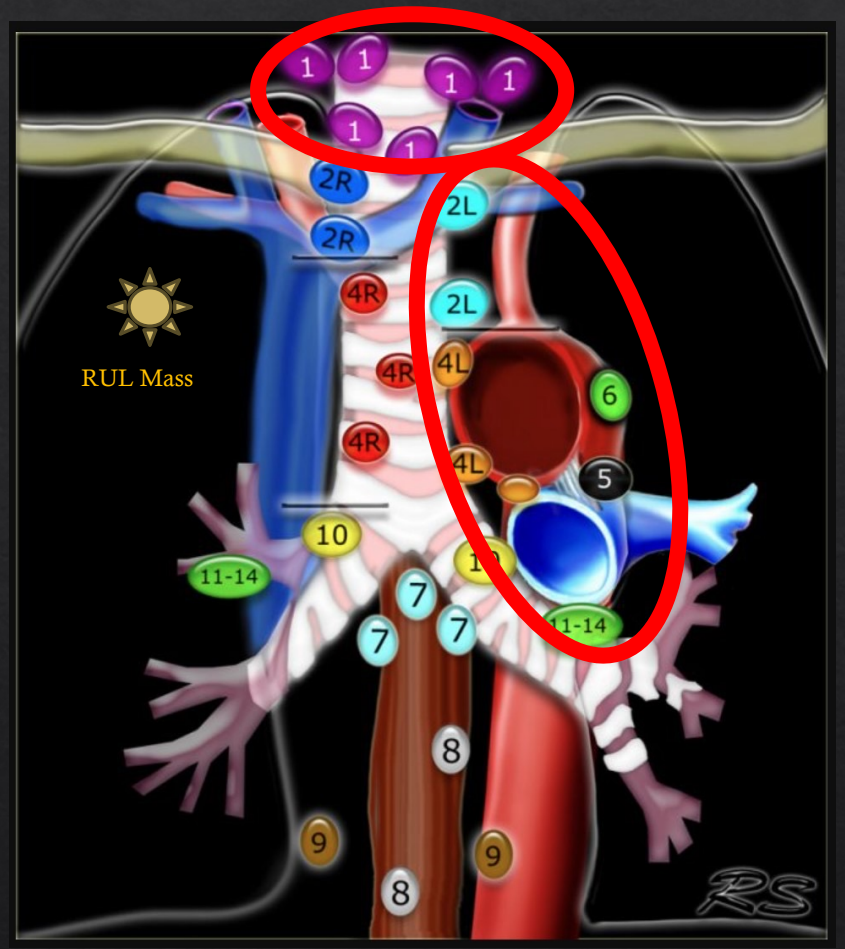



Contralateral/Supraclavicular LNs

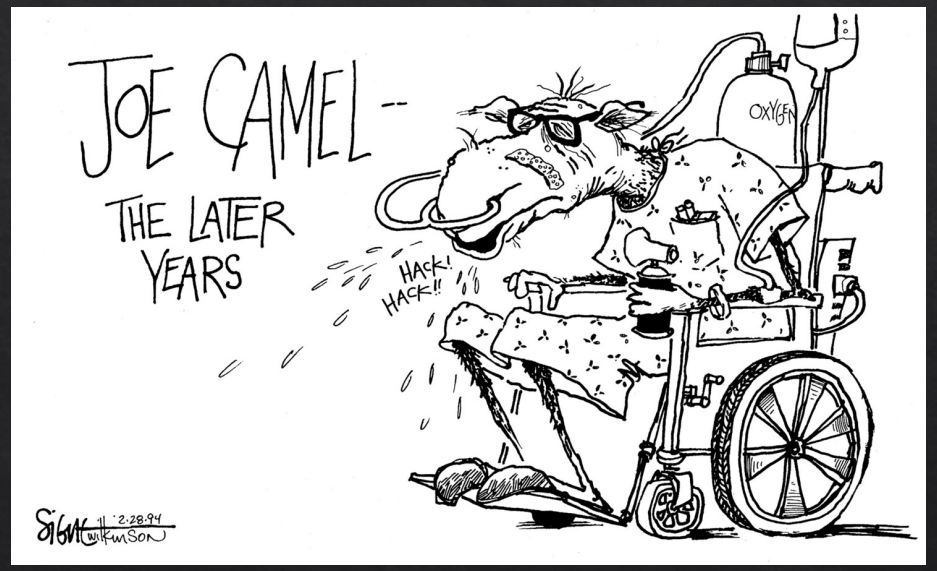



Non-surgical candidates

# Unresectable Stage III




Contralateral/Supraclavicular LNs




Non-surgical candidates

# PACIFIC: Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study in unresectable stage III NSCLC

- Patients with stage III, locally advanced, unresectable NSCLC who have not progressed following definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- Estimated life expectancy of ≥12 weeks
- Archived tissue was collected

**All-comers population**

1–42 days post-cCRT

R

2:1 randomization, stratified by age, sex, and smoking history
N=713

**Durvalumab**
**10 mg/kg q2w for up to 12 months**
**N=476**

**Placebo**
**10 mg/kg q2w for up to 12 months**
**N=237**

**Co-primary endpoints**

- PFS by BICR using RECIST v1.1*
- OS

**Key secondary endpoints**

- ORR (per BICR)
- DoR (per BICR)
- Safety and tolerability
- PROs

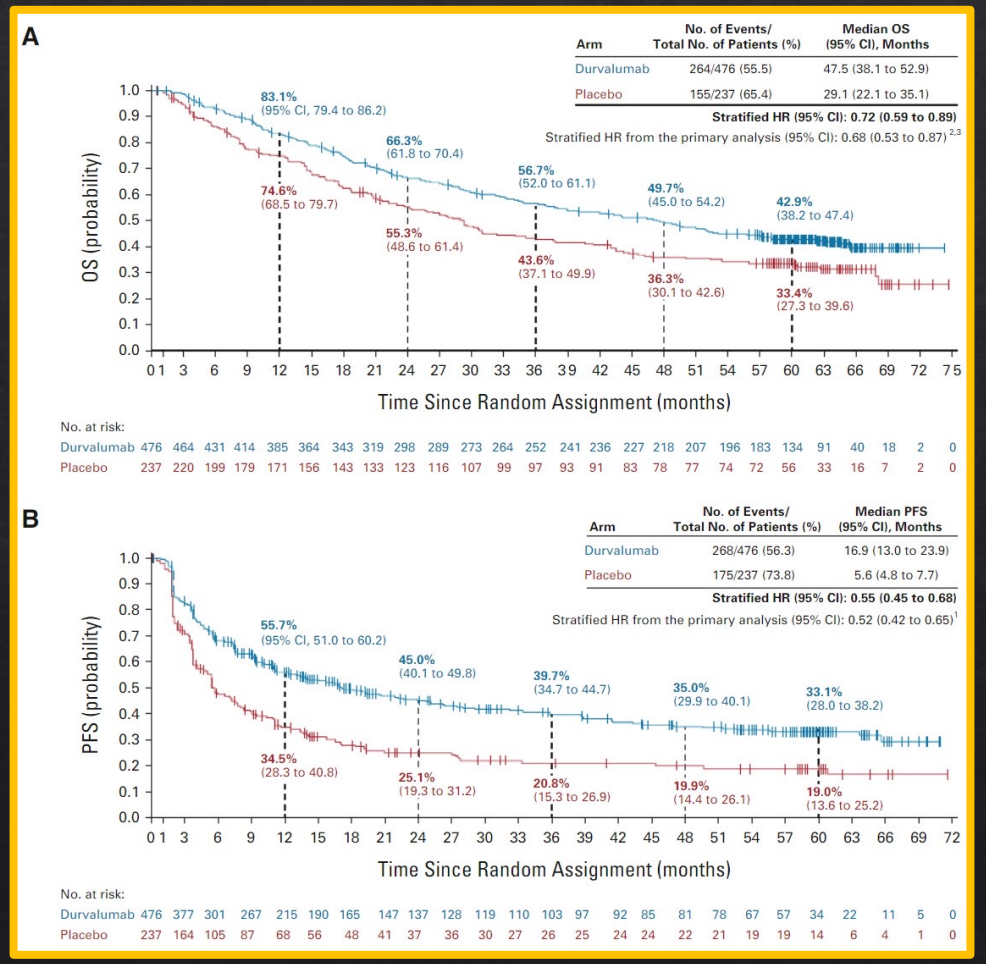
*Defined as the time from randomization (which occurred up to 6 weeks post-cCRT) to the first documented event of tumor progression or death in the absence of progression.
**ClinicalTrials.gov number: NCT02125461** BICR, blinded independent central review; cCRT, concurrent chemoradiation therapy; DoR, duration of response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q2w, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization

Paz-Ares L et al. Ann Oncol 2017;28(suppl 5): Abstr LBA1.

# PACIFIC trial

## 5 yr outcome

## Overall Survival




Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemotherapy in Stage III Non-Small-Cell Lung Cancer. Spigel DR et al., JCO. 2022: 40;1301.

# Summary of Immunotherapy Options in Early Stage and Locally Advanced NSCLC

## CheckMate 816
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Nivolumab

↓

Surgery

78% OS at 36 mos
57% EFS at 36 mos

## AEGEAN*
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Durvalumab

↓

Surgery

73% EFS at 12 mos
63% EFS at 24 mos

## KEYNOTE 671*
Resectable Stage II-III

Neoadjuvant chemotherapy
+
Pembrolizumab

↓

Surgery

73% EFS at 12 mos
62% EFS at 24 mos

## IMpower010
Resectable Stage II-III

Surgery

↓

Adjuvant Chemotherapy

↓

Atezolizumab x 12 mos
(PDL-1 ≥1%)

82% OS at 36 mos
75% DFS at 36 mos

## PACIFIC
Unresectable Stage III

Definitive Chemo/XRT
(Stable or PR/CR)

↓

Durvalumab x 12 mos

57% OS at 36 mos
43% OS at 60 mos