NCCN Guidelines: Adjuvant Therapy for Patients with Completely Resected (R0) Stages I-III NSCLC

NCCN Recommendation:

Patients with stages IB-IIIA, IIIB [T3,N2] NSCLC should receive *EGFR*, *ALK*, and PD-L1 testing.

NCCN Management Recommendations	
Stage IB (R0)	Observe or Chemotherapy for high-risk patients followed by **osimertinib** (*EGFR* exon 19 deletion or exon 21 L858R)[1]
Stage IIA (R0)	Observe or Chemotherapy for high-risk patients followed by **atezolizumab**[2] or **pembrolizumab**[3] or **osimertinib** (*EGFR* exon 19 deletion or exon 21 L858R)[1]
Stage IIB (R0)	Chemotherapy (category 1) followed by **atezolizumab**[2] or **pembrolizumab**[3] or **osimertinib** (*EGFR* exon 19 deletion or exon 21 L858R)[1]
Stages IIIA-IIIB (R0)	Chemotherapy (category 1) followed by **atezolizumab**[2] or **pembrolizumab**[3] or **osimertinib** (*EGFR* exon 19 deletion or exon 21 L858R)[1] or Sequential chemotherapy and consider radiation therapy

[1]**Osimertinib**: For patients with *EGFR* exon 19 deletion or exon 21 L858R mutations who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy.

[2]**Atezolizumab**: For patients with PD-L1 ≥1% and negative for *EGFR* exon 19 deletion or exon 21 L858R mutations or *ALK* rearrangements who received previous adjuvant chemotherapy.

[3]**Pembrolizumab**: For patients whose tumors are negative for *EGFR* exon 19 deletion or exon 21 L858R mutations or *ALK* rearrangements who received previous adjuvant chemotherapy. Benefit for patients with PD-L1 <1% is unclear.

EGFR, epidermal growth factor receptor; PD-L1, programmed death-ligand 1.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 3.2023. Updated April 13, 2023. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450

Osimertinib as Adjuvant Therapy for Resected *EGFR* Mutation-Positive NSCLC

ADAURA

Global, randomized, double-blind, phase 3 trial

- Completely resected *EGFR* mutation-positive stages IB-IIIA
  - 55% exon 19 deletion, 45% L858R, 1% T790M (1 patient)
- 60% received adjuvant chemotherapy

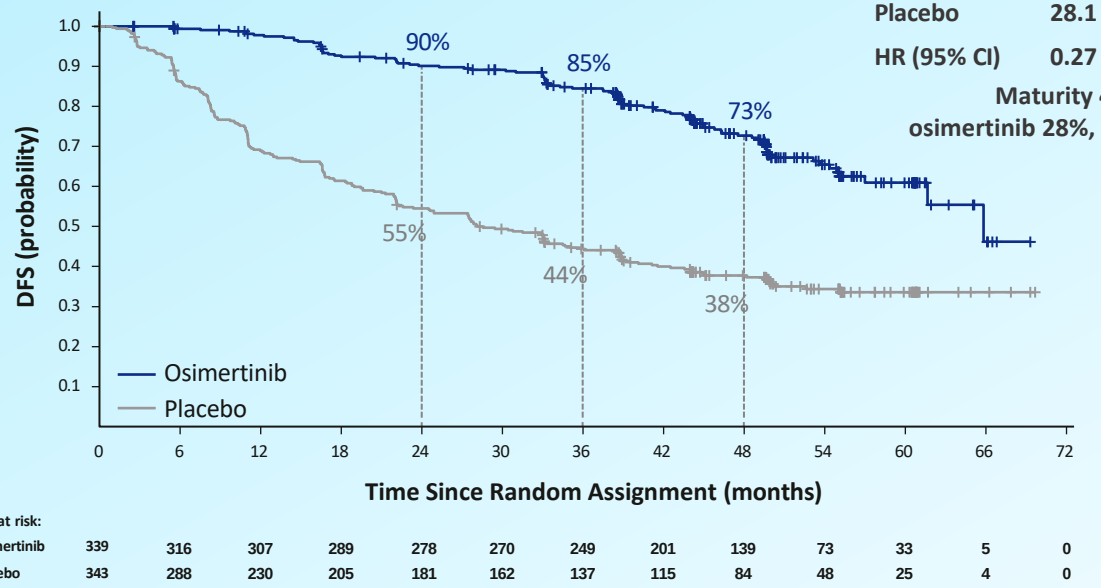
Patients alive and disease-free at 48 months

Osimertinib: **73%** (95% CI, 67-78)
Placebo: **38%** (95% CI, 32-43)

Disease-Free Survival

Median DFS, months (95% CI)	
Osimertinib	65.8 (61.7 to NC)
Placebo	28.1 (22.1 to 35.0)
HR (95% CI)	0.27 (0.21 to 0.34)

Maturity 45%: osimertinib 28%, placebo 62%



Results updated as of April 11, 2022, data cutoff

FDA approved Dec. 2020 for adjuvant therapy after tumor resection in patients with NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 L858R mutations

EGFR, epidermal growth factor receptor; DFS, disease-free survival; HR, hazard ratio; NC, not calculated.

Wu Y-L et al. *N Engl J Med* 2020;383:1711-1723; Herbst RS et al. *J Clin Oncol*. 2023;41:1830-1840; FDA Approved Drugs: Oncology (Cancer) / Hematologic Malignancies Approval Notifications /Oncology (Cancer) Approvals & Safety Notifications. Reviewed June 20, 2023. Accessed June 20, 2023. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Atezolizumab as Adjuvant Therapy for Resected PD-L1 Positive (TC ≥1%) NSCLC

IMpower010

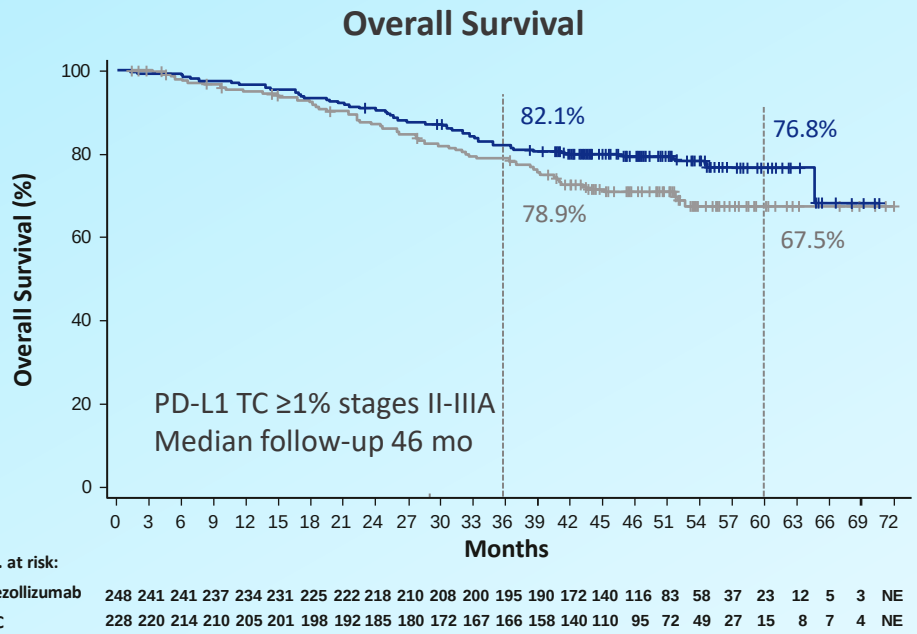
Global, randomized, open label, phase 3 trial

- Completely resected stages IB-IIIA NSCLC
- All results shown here are for stages II-IIIA PD-L1-positive population
- 99% received adjuvant chemotherapy

Initial results reported 2021

	Atezolizumab	BSC
mDFS (mo)	NE	35.3
HR for disease recurrence or death = 0.66 (95% CI, 0.50–0.88)		
DFS at 24 months	75%	61%

Updated results presented at World Conference on Lung Cancer (WCLC) 2022



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

FDA approved Oct. 2021 for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA NSCLC whose tumors have PD-L1 expression on ≥ 1% of tumor cells

PD-L1, programmed death-ligand 1; BSC, best supportive care; mDFS, median disease-free survival; HR, hazard ratio; mo, months; NE, not evaluable; NR, not reached; TC, tumor cells. Felip E et al. *Lancet* 2021;398:1344-1357; Felip E et al. Presented WCLC 2022; Abstract PL03.09; FDA Approved Drugs: Oncology (Cancer) / Hematologic Malignancies Approval Notifications /Oncology (Cancer) Approvals & Safety Notifications. Reviewed June 20, 2023. Accessed June 20, 2023. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Pembrolizumab as Adjuvant Therapy for Resected NSCLC

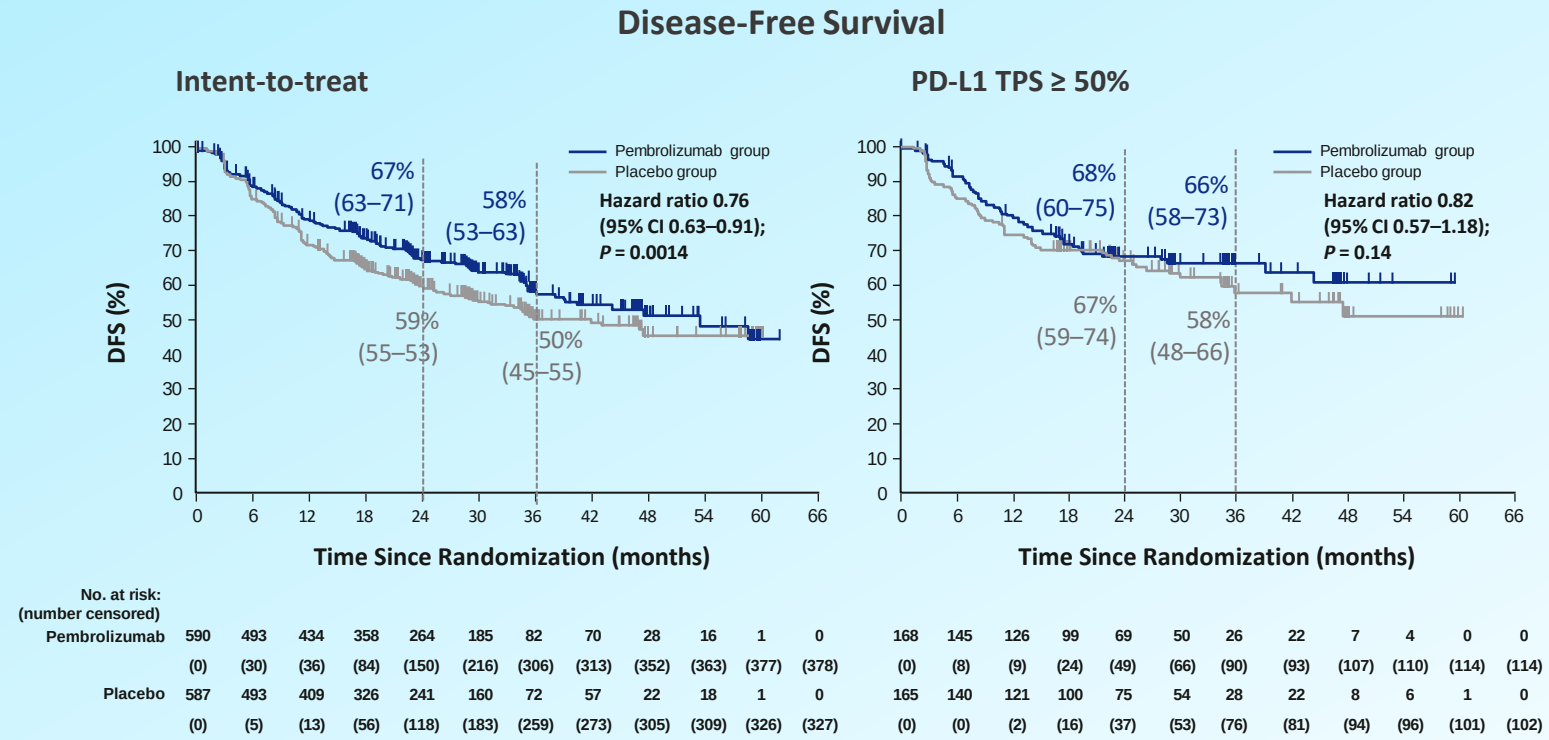
KEYNOTE-091

Global, randomized, triple blind, phase 3 trial

- Completely resected stages IB-IIIA NSCLC
- 86% received adjuvant chemotherapy

	Pembrolizumab	Placebo
mDFS (mo)	53.6	42.0
HR for disease recurrence or death = 0.76 (95% CI, 0.63–0.91)		
DFS at 24 months	67%	59%

35.6 mo follow-up, intent-to-treat population



FDA approved Jan. 2023 for adjuvant treatment following resection and platinum-based chemotherapy for stage IB (T2a ≥4 cm), II, or IIIA NSCLC

PD-L1, programmed death-ligand 1; HR, hazard ratio; mDFS, median disease-free surival; mo, months; TPS, tumor proportion score.

O'Brien M et al. *Lancet Oncol*. Oct 2022;23:1274-1286; FDA Approved Drugs: Oncology (Cancer) / Hematologic Malignancies Approval Notifications /Oncology (Cancer) Approvals & Safety Notifications. Reviewed June 20, 2023. Accessed June 20, 2023. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm.