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Immunotherapy for early-stage, resectable NSCLC: From clinical trial data to guidelines

Practice aid for non-small cell lung cancer

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Neoadjuvant immunotherapy for patients with NSCLC

Neoadjuvant immunotherapy: Phase III data[1,2]

CheckMate 816 trial (NCT02998528): 4-year update

- Neoadjuvant nivolumab plus Pt-ChT in resectable lung cancer

- Stage IB (≥4 cm) to IIIA resectable NSCLC
- 1:1 Randomization
- Nivolumab (360 mg) + Pt-ChT vs Pt-ChT alone
- Q3W for 3 weeks before surgery

	Nivolumab + Pt-ChT (n=179)	Pt-ChT alone (n=179)
mEFS (months)	43.8	18.4
4-year EFS rate	49%	38%
mOS (months)	Not reached	Not reached
4-year OS rate	71%	58%

- **Neoadjuvant nivolumab plus chemotherapy resulted in sustained EFS and OS benefit vs chemotherapy alone over time in patients with resectable NSCLC**
- **Greater benefit in patients with tumour PD-L1 expression ≥1% than <1%**

Guidelines for neoadjuvant immunotherapy[3]

NCCN (Version 6 - 14 June 2024)

- All patients should be evaluated for preoperative therapy, with strong consideration for nivolumab or pembrolizumab + chemotherapy for patients with tumours ≥4 cm or node positive and no contraindications to immune checkpoint inhibitors
- Neoadjuvant therapy should NOT be used to attempt to induce resectability in patients who do not already meet criteria for resectability on initial evaluation
- Test for PD-L1 status, *EGFR* mutations and *ALK* rearrangements (stages IB–IIIA, IIIB [T3, N2]). PD-L1 status can be incorporated with other clinical factors to determine patients who may benefit from induction chemotherapy and immunotherapy

Adjuvant immunotherapy for patients with NSCLC

Adjuvant immunotherapy: Phase III data

Agent	**Pembrolizumab[4]**	**Atezolizumab[5,6]**	
Comparator(s)	**Placebo**	**Best supportive care***	
Study	**PEARLS/KEYNOTE-091** (NCT02504372)	**IMpower010** (NCT02486718)	
Population	Resected stage IB (T ≥4 cm) to IIIA NSCLC (N=1,010)	Resected stage IB (T ≥4 cm) to IIIA NSCLC (N=1,005)	
Efficacy	Median FU: 37.4 months Pembrolizumab (n=506) **mDFS: 58.7 months** Placebo group (n=504) **mDFS: 34.9 months**	Median FU: 32.8 months[5] Atezolizumab (n=507) **mDFS: NE** BSC (n=498) **mDFS: 35.3 months**	Median FU: 65.0 months[6] Atezolizumab (n=248) **mDFS: 68.5 months** BSC (n=228) **mDFS: 37.3 months**
		(In patients with stage II–IIIA NSCLC and PD-L1 ≥1%)	

Guidelines for adjuvant immunotherapy: NCCN (Version 6 - 14 June 2024)[3]

- Atezolizumab as an adjuvant therapy option for eligible patients with completely resected stage IIB–IIIA, stage IIIB (only T3, N2), or high-risk stage IIA NSCLC and PD-L1 ≥1%, negative for *EGFR* aberrations or *ALK* rearrangements, who have previously received adjuvant chemotherapy
- Pembrolizumab as an adjuvant therapy option following adjuvant chemotherapy for eligible patients with completely resected early-stage NSCLC
- Adjuvant chemotherapy followed by atezolizumab, pembrolizumab or osimertinib for eligible patients with the appropriate biomarkers, negative surgical margins, and stage IIB disease, including T1abc–T2a, N1; T2b, N1; or T3, N0 disease
- For stage IIIA superior sulcus tumours (T4 extension, N0–1) that become resectable after preoperative concurrent chemoradiation, resection followed by chemotherapy is recommended and then atezolizumab, pembrolizumab or osimertinib, depending on biomarker status

Direct comparisons between trials should not be made due to differences in trial design.

*Included observation and regular scans for disease recurrence

Combining pre- and postoperative immunotherapy for patients with NSCLC

Perioperative immunotherapy: Phase III data

	Pembrolizumab + chemotherapy[7]	Nivolumab + chemotherapy[8]	Durvalumab + chemotherapy[9]
Agent			
Comparator(s)	**Placebo + chemotherapy**	**Placebo + chemotherapy**	**Placebo + chemotherapy**
Study	**KEYNOTE-671 (**NCT03425643)	**CheckMate 77T** (NCT04025879)	**AEGEAN** (NCT03800134)
Population	Resectable stage II–IIIB NSCLC (N=797)	Resectable stage IIA–IIIB NSCLC (N=461)	Resectable stage II–IIIB NSCLC (N=802)
Efficacy	Pembrolizumab group (n=397) **24-month EFS: 62.4%** **24-month OS: 80.9%** **PCR: 18.1%** Placebo group (n=400) **24-month EFS: 40.6%** **24-month OS: 77.6%** **PCR: 4.0%** **EFS HR: 0.58 (95% CI, 0.46–0.72; p<0.001)**	Nivolumab group (n=229) **18-month EFS: 70.2%** **PCR: 25.3%** Placebo group (n=232) **18-month EFS: 50.0%** **PCR: 4.7%** **EFS HR: 0.58 (97.36% CI, 0.42–0.81; p<0.001)**	Durvalumab group (n=400) **24-month EFS: 63.3%** **PCR: 17.2%*** Placebo group (n=402) **24-month EFS: 52.4%** **PCR: 4.3%*** **EFS HR: 0.68 (95% CI, 0.53–0.88; p<0.004)**

Biomarker testing

- NCCN guidelines recommend testing for PD-L1 status, *EGFR* mutations and *ALK* rearrangements for patients with stages IB–IIIA, IIIB [T3,N2][3]
  - Patients with known *EGFR* mutations or *ALK* rearrangements were excluded from, or enrolled in limited numbers in pivotal trials for peri-operative immunotherapy[7–9]
  - Based on the limited data in patients with *EGFR* mutations or *ALK* rearrangements, NCCN guidelines recommend exclusion of these biomarkers, at a minimum, prior to consideration for neoadjuvant immuno-chemotherapy[3]

Direct comparisons between trials should not be made due to differences in trial design.
***Interim analysis of data from 402 patients.

Abbreviations and references

Abbreviations

BSC, best supportive care; CI, confidence interval; DFS, disease free survival; EFS, event free survival; EGFR, epidermal growth factor receptor; FU, follow-up; HR, hazard ratio; mDFS, median DFS; mEFS, median EFS; mOS, median OS; NCCN, National Comprehensive Cancer Network; NE, non-estimable; NSCLC, non-small cell lung cancer; OS, overall survival; PCR, pathological complete response; PD-L1, programmed death-ligand 1; Pt-ChT, platinum-based chemotherapy; Q3W, every three weeks.

References

1. Forde PM, et al. *N Engl J Med*. 2022;386:1973–85.
2. Spicer J, et al. Presented at: ASCO Annual Meeting, Chicago, Il, USA. 31 May–4 June 2024. Abstr. LBA8010.
3. NCCN. Clinical Practice Guidelines in Oncology 2024. Non-small cell lung cancer. Version 6.2024. Available at: www.nccn.org/professionals/physician_gls/pdf/nscl.pdf (accessed 20 June 2024).
4. Oselin K, et al. *J Clin Oncol* 2023;41;8520.
5. Felip E, et al. *Lancet*. 2021;398:1344–57.
6. Wakelee HA, et al. Presented at: ASCO Annual Meeting, Chicago, Il, USA. 31 May–4 June 2024. Abstr. LBA8035.
7. Wakelee H, et al. *N Engl J Med*. 2023;389:491–503.
8. Cascone T, et al. *N Engl J Med.* 2024;390:1756–69.
9. Heymach JV, et al. *N Engl J Med.* 2023;389:1672–84.