

Non-Small Cell Lung Cancer: The Emerging Use of Immune Checkpoint Inhibitors in the Neoadjuvant Setting

REFERENCES

1. Ahren E, Solomon BJ, Hui R, et al. Neoadjuvant immunotherapy for non-small cell lung cancer: right drugs, right patient, right time? *J Immunother Cancer*. 2019;9(6):e002248. doi:10.1136/jitc-2020-002248
2. Cancer stat facts: lung and bronchus cancer. National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Program. Accessed March 7, 2022. www.seer.cancer.gov
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. *Non-Small Cell Lung Cancer*, v3.2022.
4. Detterbeck FC. The eight edition TNM stage classification for lung cancer: what does it mean on main street? *J Thorac Cardiovasc Surg* 2018;155(1):356-359. doi:10.1016/j.jtcvs.2017.08.138
5. Arriagada R, Bergman B, Dunant D, et al. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small cell-lung cancer. *N Engl J Med*. 2004;350(4):351-360. doi:10.1056/NEJMoa031644
6. Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. *N Engl J Med*. 2005;352(25):2589-2597. doi:10.1056/NEJMoa043623
7. Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIa non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. *Lancet Oncol*. 2006;7(9):719-727. doi:10.1016/S1470-2045(06)70804-X
8. Strauss GM, Herndon JE, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. *J Clin Oncol*. 2008;26(31):5043-5051. doi:10.1200/JCO.2008.16.4855
9. Felip E, Rosell R, Maestre JA, et al. Preoperative chemotherapy plus surgery versus surgery plus adjuvant chemotherapy versus surgery alone in early-stage non-small-cell lung cancer. *J Clin Oncol*. 2010;28(19):3138-3145. doi:10.1200/JCO.2009.27.6204
10. Pisters KMW, Vallières E, Crowley JJ, et al. Surgery with or without preoperative paclitaxel and carboplatin in early-stage non-small-cell lung cancer: Southwest Oncology Group Trial S9900, an intergroup, randomized, phase III trial. *J Clin Oncol*. 2010;28(11):1843-1849. doi:10.1200/JCO.2009.26.1685
11. Gilligan D, Nicolson M, Smith I, et al. Preoperative chemotherapy in patients with resectable non-small cell lung cancer: results of the MRC LU22/NVALT 2/EORTC 08012 multicentre randomised trial and update of systematic review. *Lancet*. 2007;369(9577):1929-1937. doi:10.1016/S0140-6736(07)60714-4
12. Scagliotti GV, Pastorino U, Vansteenkiste JF, et al. Randomized phase III study of surgery alone or surgery plus preoperative cisplatin and gemcitabine in stages IB to IIIa non-small-cell lung cancer. *J Clin Oncol*. 2012;30(2):172-178. doi:10.1200/JCO.2010.33.7089
13. Depierre A, Milleron B, Moro-Sibilot D, et al. Preoperative chemotherapy followed by surgery compared with primary surgery in resectable stage I (except T1N0), II, and IIIa non-small-cell lung cancer. *J Clin Oncol*. 2002;20(1):247-253. doi:10.1200/JCO.2002.20.1.247

14. Chen X, Kewei M. Neoadjuvant therapy in lung cancer: what is most important: objective response rate or major pathological response? *Curr Oncol*. 2021;28(5):4129-4138. doi:10.3390/curroncol28050350
15. Berghmans T, Paesmans M, Meert AP, et al. Survival improvement in resectable non-small cell lung cancer with (neo)adjuvant chemotherapy: results of a meta-analysis of the literature. *Lung Cancer*. 2005;49(1):13-23. doi:10.1016/j.lungcan.2005.01.002
16. Burdett S, Stewart LA, Rydzewska L, et al. A systematic review and meta-analysis of the literature: chemotherapy and surgery versus surgery alone in non-small cell lung cancer. *J Thorac Oncol*. 2006;1(7):611-621.
17. Song WA, Zou NK, Wang W, et al. Survival benefit of neoadjuvant chemotherapy in non-small cell lung cancer: an updated meta-analysis of 13 randomized control trials. *J Thorac Oncol*. 2010;5(4):510-516. doi:10.1097/JTO.0b013e3181cd3345
18. Pataer A, Kalhor N, Correa AM, et al. Histopathologic response criteria predict survival of patients with resected lung cancer after neoadjuvant chemotherapy. *J Thorac Oncol*. 2012;7(5):825-832. doi:10.1097/JTO.0b013e318247504a
19. Hellmann M, Chaft JE, William Jr WN, et al. Pathologic response after neoadjuvant chemotherapy in resectable non-small-cell lung cancers: proposal for the use of "major pathologic response" as a surrogate endpoint. *Lancet Oncol*. 2014;15(1):e42-e50. doi:10.1016/S1470-2045(13)70334-6
20. Antonia SJ, Villegas A, Daniel D, et al. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. *N Engl J Med*. 2018;379(24):2342-2350. doi:10.1056/NEJMoa1809697
21. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N Engl J Med*. 2017;377(20):1919-1929. doi:10.1056/NEJMoa1709937
22. Felip E, Altorki N, Zhou C, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. *Lancet*. 2021;398(10308):1344-1357. doi:10.1016/S0140-6736(21)02098-5
23. Versluis JM, Long GV, Blank CU. Learning from clinical trials of neoadjuvant checkpoint blockade. *Nat Med*. 2020;26(4):475-484. doi:10.1038/s41591-020-0829-0
24. Grellier L, Tomasini P, Barlesi F. The clinical utility of tumor mutational burden in non-small cell lung cancer. *Transl Lung Cancer Res*. 2018;7(6):639-646. doi:10.21037/tlcr.2018.10.08
25. Palmero R, Vilariño N, Navarro-Martín A, Nadal E. Induction treatment in patients with stage III non-small cell lung cancer. *Transl Lung Cancer Res*. 2021;10(1):539-554. doi:10.21037/tlcr-20-420
26. Forde PM, Spicer J, Lu S, et al. Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment (tx) for resectable (IB-IIIA) non-small cell lung cancer (NSCLC) in the phase 3 CheckMate 816 trial. In: Proceedings of the American Association of Cancer Research Annual Meeting 2021; April 14-15 and May 17-21, 2021. Philadelphia, PA; AACR 2021. *Cancer Res*. 2021;81(suppl 13):Abstract CT003. <https://doi.org/10.1158/1538-7445.AM2021-CT003>
27. Clinical Trials.gov Identifier: NCT03425643. Efficacy and safety of pembrolizumab (MK-3475) with platinum doublet chemotherapy as neoadjuvant/adjuvant therapy for participants with resectable stage II, IIIA, resectable IIIB (T3-4N2) non-small cell lung cancer (MK3475-671/KEYNOTE-671). Updated November 29, 2021. Accessed April 15, 2022. <https://clinicaltrials.gov/ct2/show/NCT03425643>
28. Clinical Trials.gov Identifier: NCT03456063. A study of neoadjuvant atezolizumab plus chemotherapy versus placebo plus chemotherapy in patients with resectable stage II, IIIA, or select IIIB non-small

cell lung cancer (IMpower030). Updated March 29, 2022. Accessed April 15, 2022.

<https://clinicaltrials.gov/ct2/show/NCT03456063>

29. Clinical Trials.gov Identifier: NCT03800134. A study of neoadjuvant/adjuvant durvalumab for the treatment of patients with non-small cell lung cancer (AEGEAN). Updated March 11, 2022. Accessed April 15, 2022. <https://www.clinicaltrials.gov/ct2/show/NCT03800134>
30. Clinical Trials.gov Identifier: NCT04025879. A study of neoadjuvant chemotherapy plus nivolumab versus neoadjuvant chemotherapy plus placebo, followed by surgical removal and adjuvant treatment with nivolumab or placebo for participants with surgically removable early stage non-small cell lung cancer (CheckMate 77T). Updated April 1, 2022. Accessed April 15, 2022. <https://www.clinicaltrials.gov/ct2/show/NCT04025879>
31. Weinmann SC, Pisetsky DS. Mechanisms of immune-related adverse events during the treatment of cancer with immune checkpoint inhibitors. *Rheumatology (Oxford)*. 2019;58(suppl 7):vii59-vii67. doi:10.1093/rheumatology/kez308
32. Zubiri L, Allen IA, Taylor MS, et al. Immune-related adverse events in the setting of PD-1/L1 inhibitor combination therapy. *Oncologist*. 2020;25(3):e398-e404. doi:10.1634/theoncologist.2018-0883
33. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Management of Immunotherapy-Related Toxicities, v1.2022.
34. Remon J, Mezquita L, Corral J, et al. Immune-related adverse events with immune checkpoint inhibitors in thoracic malignancies: focusing on non-small cell lung cancer patients. *J Thorac Dis*. 2018;10(suppl 13):S1516-S1533. doi:10.21037/jtd.2017.12.52