



With a deep scientific understanding of Immuno-Oncology, we have expanded our research to focus on leveraging immune checkpoint pathways in hopes of potentially improving outcomes for patients with earlier stages of cancer.⁴⁰⁻⁴⁹

Active research spans multiple tumors, including some tumors that may have risk of recurrence following complete surgical resection⁴⁰⁻⁴⁸



Breast



Esophageal



GEJC



Head and neck



HCC



RCC



UC



Melanoma



NSCLC

BMS is committed to exploring the potential of Immuno-Oncology in Earlier Stages of Cancer

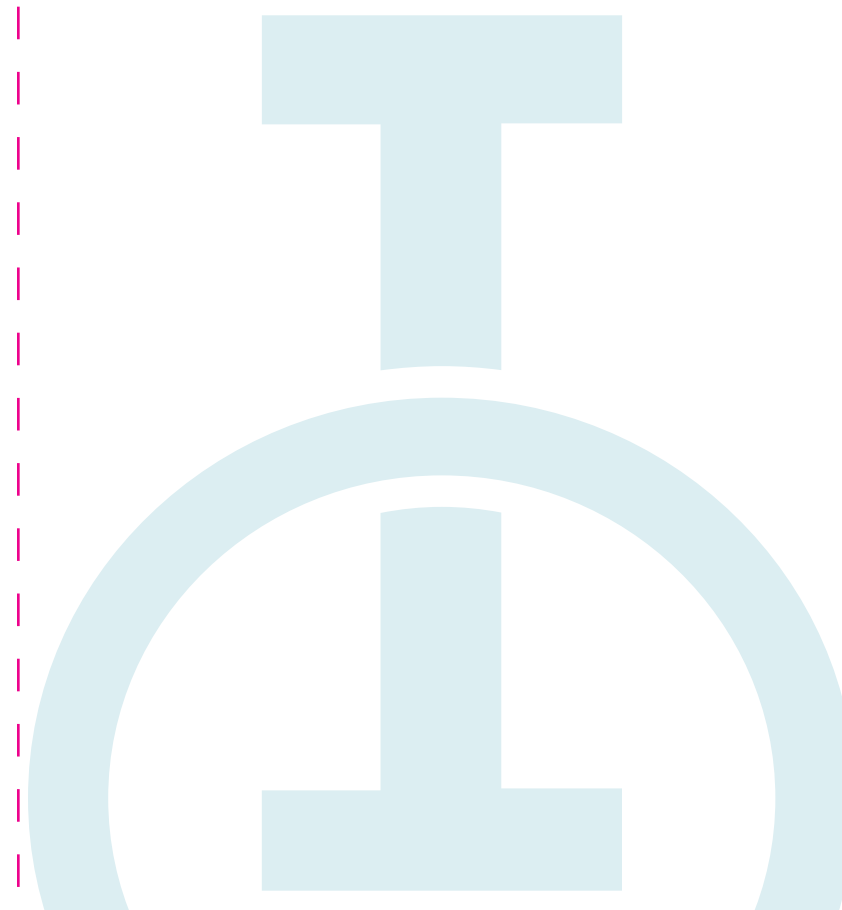
GEJC=gastroesophageal junction cancer; HCC=hepatocellular carcinoma; I-O=Immuno-Oncology; MDT=multidisciplinary team; NSCLC=non-small cell lung cancer; RCC=renal cell carcinoma; UC=urothelial cancer.

References: 1. Romano, et al. *J Clin Oncol*. 2010;28(18):3402-3047. 2. Vogel A, et al. *Ann Oncol*. 2018;29(suppl 4):iv238-iv255. 3. Taylor MD, et al. *Ann Thorac Surg*. 2012;93:1813-1821. 4. Boegemann M, Krabbe L-M. *Mini Rev Med Chem*. 2020;20:1133-1152. 5. Lou F, et al. *J Thorac Oncol*. 2013;8(12):1558-1562. 6. Gonzalez H, et al. *Genes Dev*. 2018;32:1267-1284. 7. Marin-Acevedo JA, et al. *J Hematol Oncol*. 2018;11:39. 8. Pardoll DM, et al. *Nat Rev Cancer*. 2012;12:252-264. 9. Pedicord VA, et al. *Proc Natl Acad Sci U S A*. 2011;108(1):266-271. 10. Buchbinder EI, et al. *Am J Clin Oncol*. 2016;39(1):98-106. 11. Simpson TR, et al. *J Exp Med*. 2013;210(9):1695-1710. 12. Matsuzaki J, et al. *Proc Natl Acad Sci U S A*. 2010;107(17):7875-7880. 13. Lichtenecker FS, et al. *Front Immunol*. 2018;9:385. 14. Sznol M, et al. *Clin Cancer Res*. 2013;19(5):1021-1034. 15. Versluis JM, et al. *Nat Med*. 2020;26(4):475-484. 16. Keung EZ et al. *Ann Surg Oncol*. 2018;25(7):1814-1827. 17. Bai R, et al. *Front Oncol*. 2020;10(575472):1-10. 18. Yang C, et al. *Front Immunol*. 2020;11:577869. 19. Saltz LB. *Surg Oncol Clin N Am*. 2010;19(4):819-827. 20. Amin S, et al. *BMC Cancer*. 2020;20:538. 21. Pantel K, et al. *J Natl Cancer Inst*. 1999;91(13):1113-1124. 22. Vansteenkiste J, et al. *Ann Oncol*. 2019;30:1244-1253. 23. Zhang P, et al. *Cancer Res*. 2007;67(13):6468-6476. 24. Bakos O et al. *J Immunother Cancer*. 2018;6(1):86. 25. Pandya PH, et al. *J Immunol Res*. 2016;4273943. 26. Ni Y et al. *Front Oncol*. 2023;13:1092663. 27. Metro G et al. *Expert Opin Drug Saf*. 2017;16(1):101-109. 28. Byrne EH, Fisher DE. *Cancer*. 2017;123(S11):2143-2153. 29. US Food and Drug Administration. Clinical trial endpoints for the approval of cancer drugs and biologics. Published December 2018. Accessed May 2, 2021. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-endpoints-approval-cancer-drugs-and-biologics>. 30. US Food and Drug Administration. Pathological complete response in neoadjuvant treatment of high-risk early-stage breast cancer: use as an endpoint to support accelerated approval. Published July 2020. Accessed May 2, 2021. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pathological-complete-response-neoadjuvant-treatment-high-risk-early-stage-breast-cancer-use>. 31. Punt CA, et al. *J Natl Cancer Inst*. 2007;99(13):999-1004. 32. Gyawali B, et al. *EClinicalMedicine*. 2020;21:100332. 33. Cottrell TR, et al. *Ann Oncol*. 2018;29:1853-1860. 34. Suci S, et al. *J Natl Cancer Inst*. 2018;110(1):dix133. 35. Saad ED, et al. *Lancet Oncol*. 2019;20(3):361-370. 36. Gyawali B, et al. *EClinicalMedicine*. 2021;32:100730. 37. Manguen A, et al. *Lancet Oncol*. 2013;14(7):619-626. 38. Michiels S, et al. *Lancet Oncol*. 2009;10(4):341-350. 39. NCI Dictionary of Cancer Terms. Relapse-free survival. Accessed May 7, 2021. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/relapse-free-survival>. 40. Clinicaltrials.gov. NCT04109066. Accessed May 2, 2021. 41. Clinicaltrials.gov. NCT02743494. Accessed May 2, 2021. 42. Clinicaltrials.gov. NCT03383458. Accessed May 2, 2021. 43. Clinicaltrials.gov. NCT03138512. Accessed May 2, 2021. 44. Clinicaltrials.gov. NCT02632409. Accessed May 2, 2021. 45. Clinicaltrials.gov. NCT02388906. Accessed May 2, 2021. 46. Clinicaltrials.gov. NCT02998528. Accessed May 2, 2021. 47. Clinicaltrials.gov. NCT04026412. Accessed May 2, 2021. 48. Clinicaltrials.gov. NCT03576417. Accessed May 19, 2021. 49. Berman D et al. *Pharmacol Ther*. 2015;148:132-153.

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Investigating the Potential of Immuno-Oncology in the Earlier Stages of Cancer



Immuno-Oncology research aims to harness the body's natural immune response to detect and eliminate tumor cells

- In earlier stages* of many cancer types, the **risk of recurrence** following complete surgical resection may be high¹⁻⁵



71%–85%
for melanoma
(stage IIIB
and IIIC)^{1†}



50%–70%
for
HCC^{2‡}



≤50%
for bladder
cancer
(muscle invasive)⁴

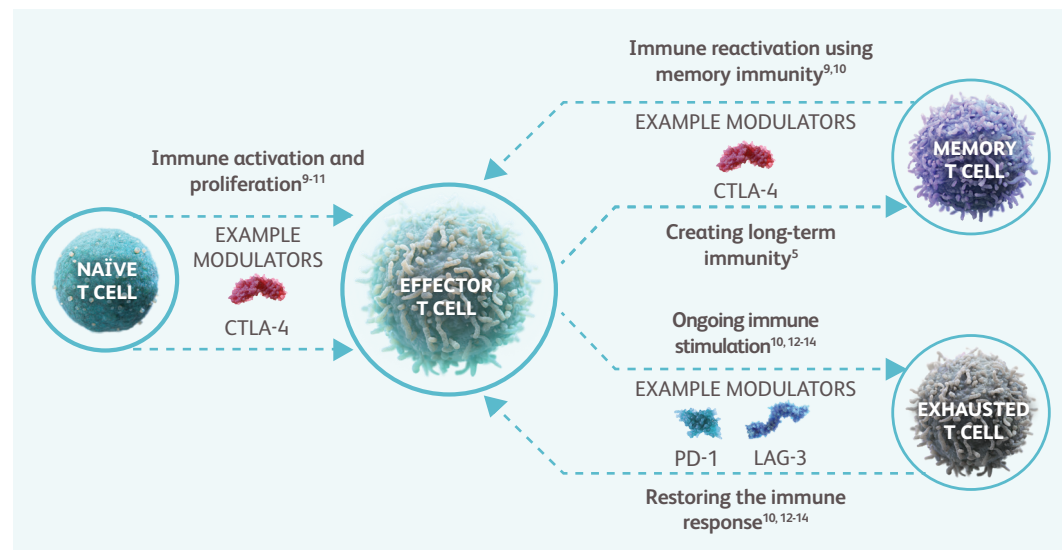


29%–47%
for lung
cancer^{3§}



38%
for
esophageal
cancer^{5||}

- Ongoing research to further understand immune pathways includes exploring how their modulation may improve antitumor immune response⁶⁻⁸

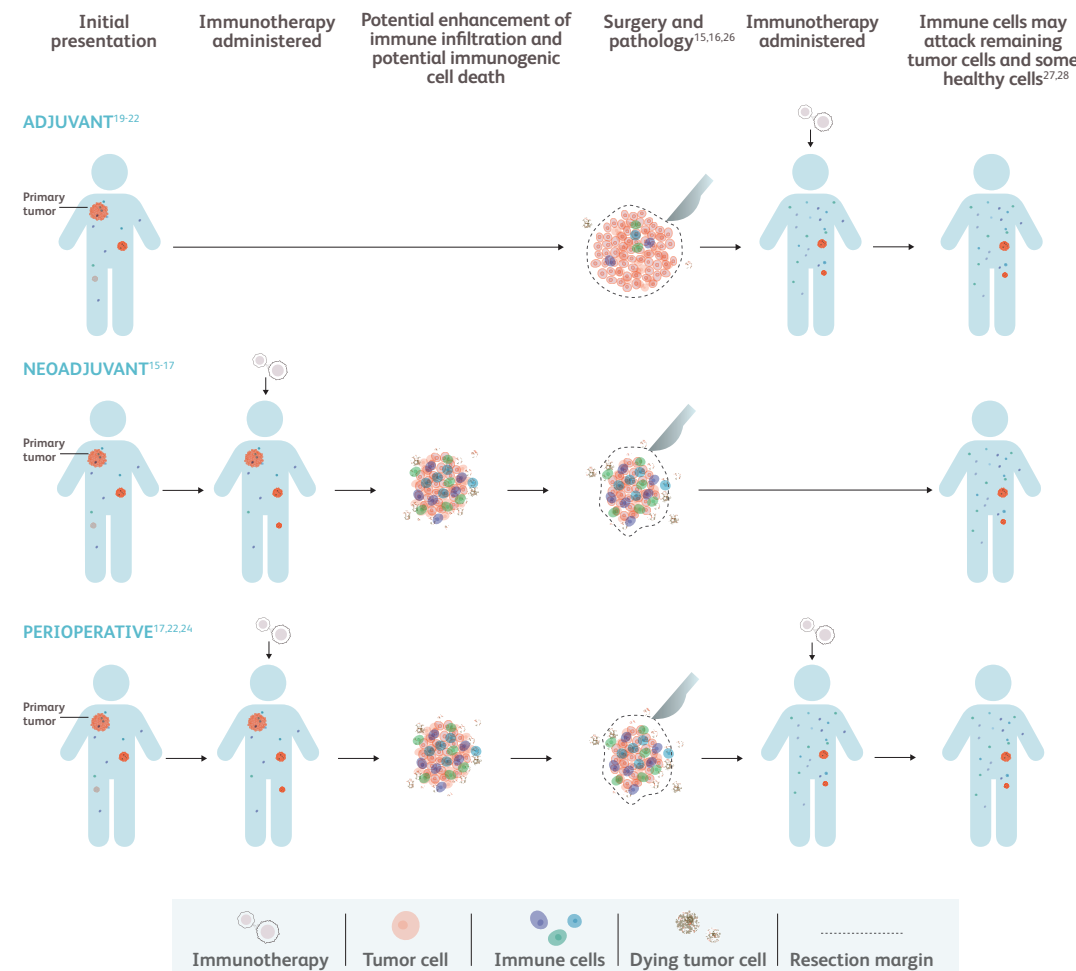


The generation of memory T cells may provide a prolonged immune response

*Earlier stages of cancer refers to tumors that are non-metastatic or resectable metastatic. †Data from a single center spanning 1998–2002. ‡Based on worldwide data, according to the ESMO Faculty for Clinical Practice Guidelines development. §Data from a single center spanning 1999–2008. ||Data from a single center spanning 1996–2010. CTLA-4=cytotoxic T-lymphocyte antigen 4; HCC=hepatocellular carcinoma; I-O=Immuno-Oncology; LAG-3=lymphocyte-activation gene 3; MDT=multidisciplinary team; PD-1=programmed death receptor-1.

Adjuvant, neoadjuvant, and perioperative immunotherapy research seeks to activate the body's natural immune response¹⁵⁻²⁴

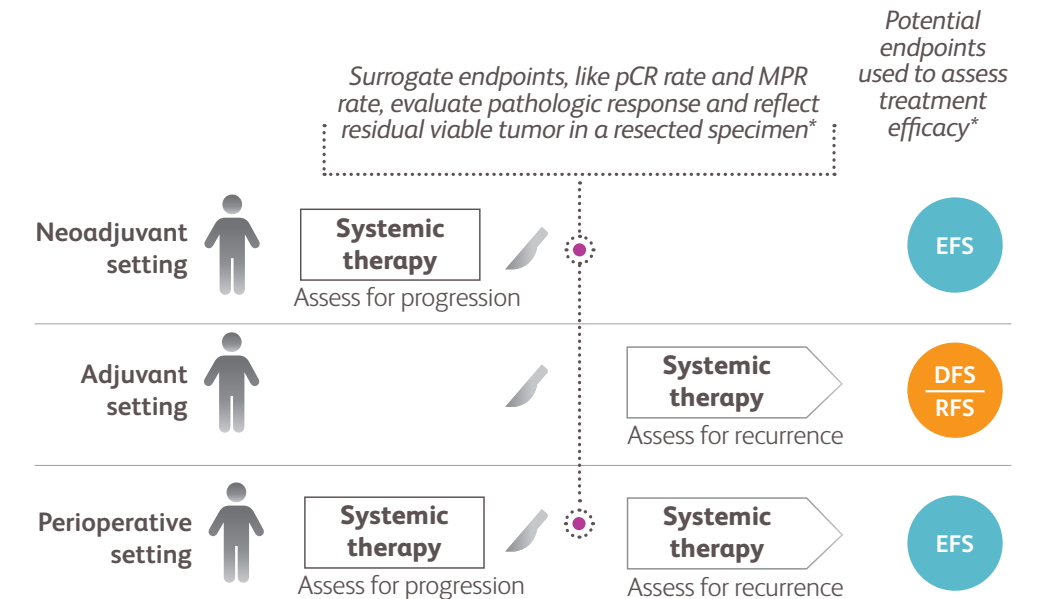
- Research is ongoing as to whether combining immunotherapy with surgery may lead to lower rates of tumor recurrence in earlier stages of cancer^{19,20,24,25}



In earlier stages of cancer, the immune system may be more intact and responsive²⁵; therefore, BMS is currently researching the potential utility of immunotherapy in this space.

Surrogate endpoints for survival may help to assess the efficacy of treatment in the neoadjuvant, adjuvant, and perioperative settings²⁹⁻³⁸

- While OS is a common endpoint in oncology, it requires a longer follow-up period. Surrogate endpoints may potentially correlate with OS.



According to research in the neoadjuvant setting, **pCR rate** and **MPR rate** may be emerging surrogate endpoints that evaluate residual tumor in a specimen^{2,4,5}

- EFS** Represents the time from when a patient is randomized (before systemic treatment and surgery) until any event, including progression of disease that precludes surgery, recurrence, or death irrespective of cause.^{29,32}
- DFS/RFS** Represents the length of time after primary treatment ends that the patient survives without any signs or symptoms of the cancer for which they were treated.³⁹

DFS=disease-free survival; EFS=event-free survival; I-O=Immuno-Oncology; MDT=multidisciplinary team; MPR=major pathologic response; OS=overall survival; pCR=pathologic complete response; RFS=recurrence-free survival.