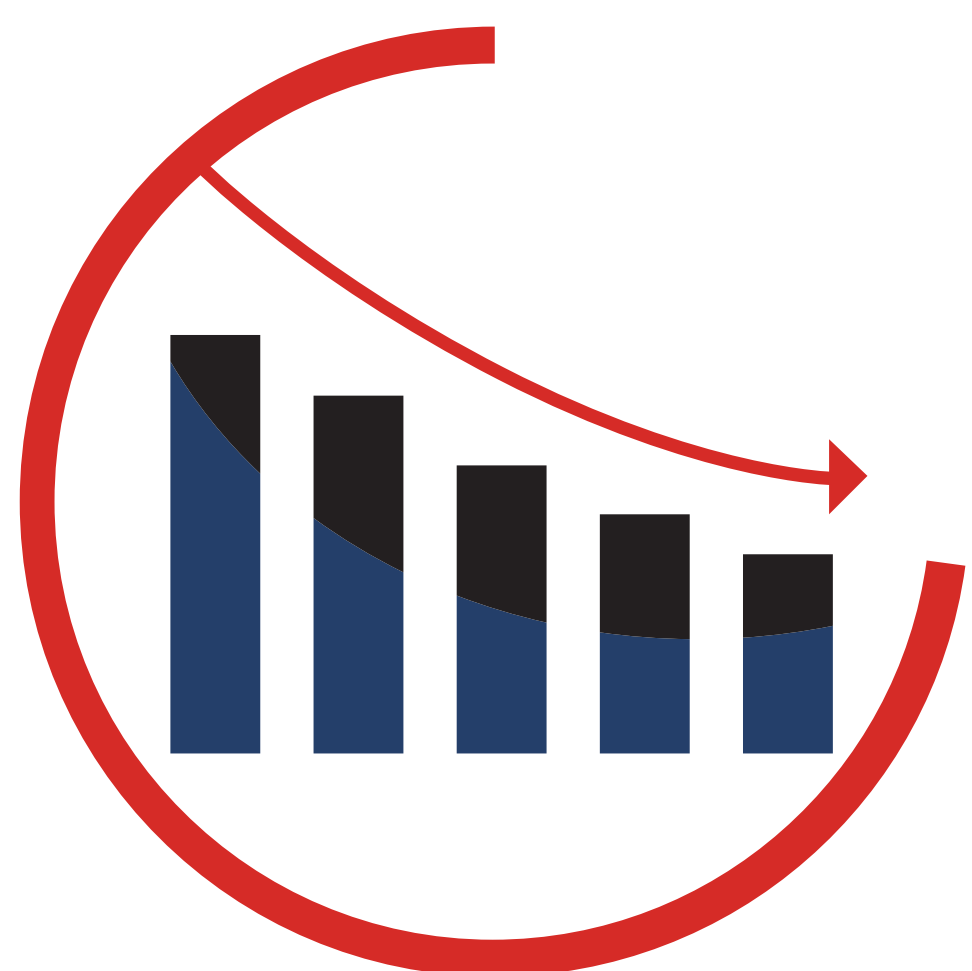


High-Risk, Early Breast Cancer:

The Importance of Surrogate Endpoints for Adjuvant Breast Cancer Clinical Trials: IDFS and DRFS

Patients with early breast cancer (EBC) are treated with curative intent¹

With access to more treatment options, mortality risk in patients with breast cancer has been significantly reduced²⁻⁴

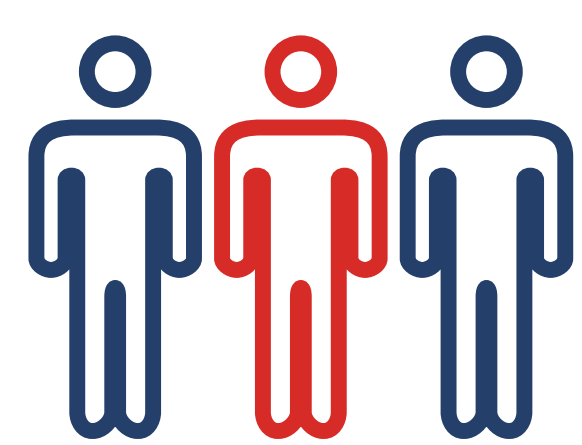


For this reason, it is not practical to rely on overall survival (OS) in adjuvant breast cancer clinical trials, as it can take decades before OS is reliably measured⁵

Defining surrogate endpoints

To observe efficacy outcomes for patients with EBC, it has become essential to define surrogate endpoints for OS. This is especially crucial in the adjuvant setting⁵

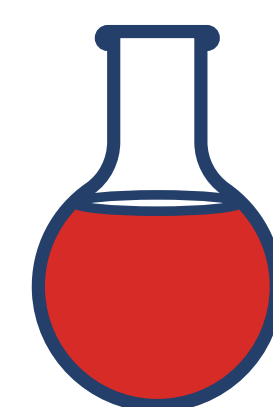
To ensure the use of standardized endpoints, careful consideration should be taken across the clinical trial lifecycle:⁵



Before trial initiation



During the trial



At analysis



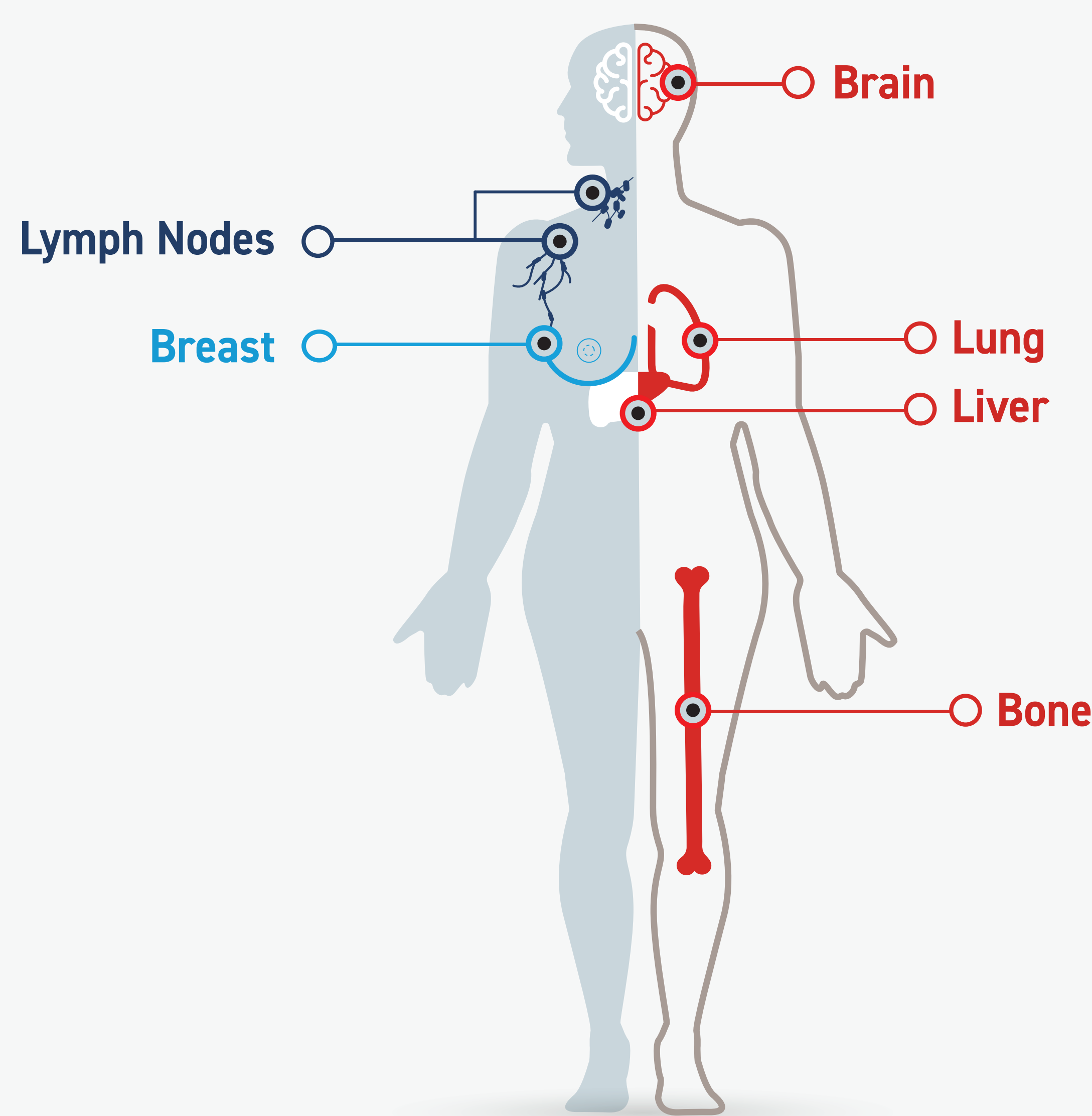
At publication

Through the development of the Standardized Definitions for Efficacy End Points (STEEP) system and other global initiatives, time-to-event endpoints have been largely standardized to mitigate inconsistencies in endpoint definitions that may confound interpretation of clinical trial results^{2,5}

Invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS) are surrogate endpoints for OS^{5,6}

IDFS is a composite endpoint that includes local, regional, and distant recurrence. DRFS emphasizes distant recurrence, or metastasis in a vital organ

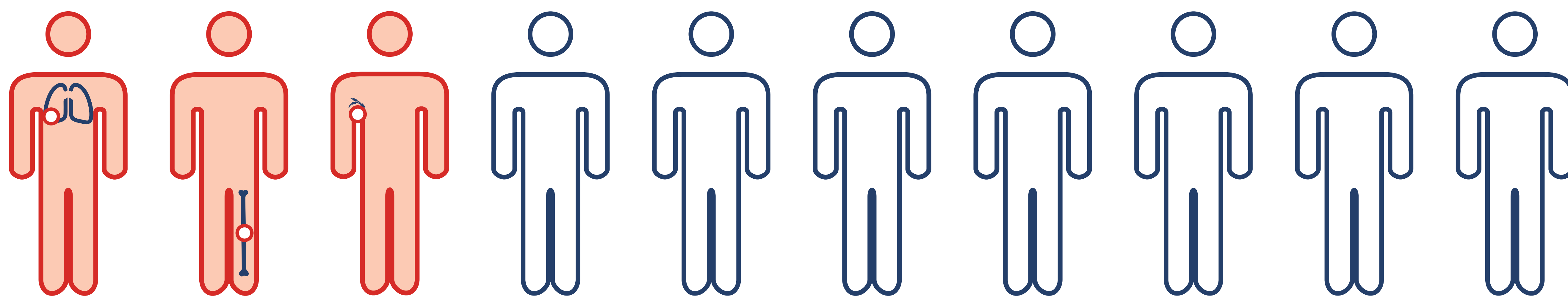
Local recurrence | Regional recurrence | Distant recurrence



Recurrence of breast cancer can be local, regional, or distant.⁷ Risk of recurrence peaks early in patients at ~2 years after primary diagnosis^{7,8}

Implications for patients with high-risk disease

Because ~30% of patients with high-risk, hormone receptor-positive (HR+)/HER2-negative (HER2-) EBC experience disease recurrence in 5 years,⁶ IDFS and DRFS are very meaningful clinical endpoints



1. Yung R, et al. *Breast Cancer Res Treat.* 2020;180(3):747-757.
 2. Gourgou-Bourgade S, et al. *Ann Oncol.* 2015;26(5):873-879.
 3. Garutti M, et al. *Cancers.* 2022;14(1898):1-17.
 4. Giaquinto AN, et al. *CA Cancer J Clin.* 2022;72(6):524-541.
 5. Hudis CA, et al. *J Clin Oncol.* 2007;25(15):2127-2132.
 6. Sheffield KM, et al. *Future Oncol.* 2022;18(21): 2667-2682.
 7. Colleoni M, et al. *J Clin Oncol.* 2016;34(9):927-935.
 8. Cheng L, et al. *Cancer Epidemiol Biomarkers Prev.* 2012;21(5):800-809.

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IDFS and DRFS: Composite Endpoints Used in Adjuvant Breast Cancer Clinical Trials^{1,2}

Both **IDFS** and **DRFS** are standardized, clinically meaningful endpoints in adjuvant breast cancer clinical trials^{1,2}

Endpoint	Local Invasive Recurrence	Regional Invasive Recurrence	Distant Recurrence	Death of Any Cause	Invasive Ipsilateral Breast Tumor Recurrence	Invasive Contralateral Breast Cancer	DCIS ^a	Second Primary Nonbreast Invasive Cancer
IDFS	✓	✓	✓	✓	✓	✓	✗	✓
DRFS	✗	✗	✓	✓	✗	✗	✗	✗

^aIncludes both ipsilateral and contralateral DCIS. DCIS, ductal carcinoma in situ.

Preventing breast cancer recurrence



As healthcare providers, we want to prevent breast cancer recurrence. Improvement in **IDFS** or **DRFS** means fewer recurrences and fewer instances of incurable metastatic disease, which are critically important to us in practice

1. Hudis CA, et al. *J Clin Oncol*. 2007;25(15):2127-2132.

2. Gourgou-Bourgade S, et al. *Ann Oncol*. 2015;26(5):873-879.