Early Breast Cancer at ASCO 2026: Trials to Watch

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Early breast cancer management sits at a crossroads: survival outcomes have improved substantially with existing regimens,1 yet questions about de-escalation in low-risk HER2-positive disease, optimal CDK4/6 inhibitor sequencing in HR-positive early-stage disease, and the durability of pathological complete response (pCR) as a surrogate endpoint remain unresolved. ASCO 2026 is expected to present mature follow-up data and new trial readouts that will directly inform adjuvant treatment decisions in clinic.

KEY TAKEAWAYS

- The Pivot: Mature survival endpoints from adjuvant CDK4/6 inhibitor and extended neoadjuvant trials in early breast cancer are anticipated, moving the conversation from surrogate markers toward overall survival data.
- The Data: Watch for overall survival and invasive disease-free survival (iDFS) readouts; pCR rates alone are no longer sufficient for regulatory or clinical decision-making in most subtypes.
- The Action: Clinicians should not change adjuvant prescribing ahead of these readouts, but should document treatment rationale carefully now, as label updates or guideline revisions from ASCO, ESMO, and NCCN may follow quickly after presentation.

The early breast cancer landscape heading into ASCO 2026 is shaped by three converging questions. First, can adjuvant CDK4/6 inhibition extend overall survival in hormone receptor-positive (HR+), HER2-negative early breast cancer, beyond the iDFS benefit already demonstrated with abemaciclib in monarchE? Second, does de-escalated HER2-directed therapy maintain efficacy while reducing toxicity in low-risk HER2-positive disease? Third, does achieving pCR after neoadjuvant chemotherapy translate into long-term survival benefit across all molecular subtypes, or does the relationship break down in HR-positive disease, as earlier meta-analyses have suggested?

These are not abstract academic disputes. Adjuvant abemaciclib (Eli Lilly) received approval in HR+, HER2-negative, node-positive early breast cancer based on iDFS data from monarchE, where the 4-year iDFS rate was 85.8% versus 79.4% in favour of the abemaciclib arm.1 The monarchE trial enrolled patients with HR+, HER2-negative, node-positive early breast cancer who had high-risk clinical and pathological features, such as four or more positive axillary lymph nodes, or one to three positive lymph nodes with either tumor grade 3 or a tumor size of at least 5 cm. Patients were randomized to receive either abemaciclib plus standard endocrine therapy or endocrine therapy alone. Overall survival data from monarchE remain immature but are expected to surface at a major 2025 or 2026 congress. Similarly, the ribociclib-based NATALEE trial reported a 3-year iDFS improvement in a broader HR+ early breast cancer population, with an iDFS rate of 90.4% versus 87.1% (HR 0.748, 95% CI 0.618 to 0.906) in the primary analysis.2 NATALEE included a wider population of HR+, HER2-negative early breast cancer patients, encompassing both node-positive

disease and node-negative disease with high-risk features. The trial design involved a three-year adjuvant ribociclib regimen, a longer duration than the two years typically studied for CDK4/6 inhibitors in this setting. Whether either agent delivers an overall survival signal will determine how aggressively oncologists pursue two years of adjuvant CDK4/6 inhibition given the cost, toxicity burden, and patient adherence challenges involved. The mechanism of action for CDK4/6 inhibitors involves blocking cyclin-dependent kinases 4 and 6, which are crucial for cell cycle progression, thereby inhibiting proliferation of cancer cells.

What the field is waiting for

In HER2-positive early breast cancer, the de-escalation question centres on whether patients achieving pCR after neoadjuvant pertuzumab and trastuzumab can safely forgo adjuvant T-DM1 or extended HER2 blockade. The COMPASS-pCR and PHERGain trials have already provided preliminary signals that biology-driven de-escalation is feasible in selected patients, with PHERGain reporting a pCR rate of 37.9% in the PET-guided cohort that received chemotherapy-free neoadjuvant treatment with trastuzumab and pertuzumab.3 The PHERGain trial specifically investigated a PET-guided de-escalation strategy for patients with HER2-positive early breast cancer, where patients with an early metabolic response to HER2-directed therapy could potentially avoid chemotherapy. This approach aims to reduce the cumulative toxicity associated with multi-agent chemotherapy while maintaining therapeutic efficacy. Long-term event-free survival data from these cohorts are anticipated. The rationale for de-escalation is particularly strong in HER2-positive disease, where highly effective targeted therapies have significantly improved outcomes, leading to a desire to minimize overtreatment in patients who respond well.

The TRIPLE-B and other triple-negative breast cancer (TNBC) adjuvant trials involving immunotherapy maintenance after neoadjuvant chemoimmunotherapy also remain in active follow-up. The approval of pembrolizumab (Merck) in high-risk early TNBC was built on event-free survival data from KEYNOTE-522, where the 3-year EFS rate was 84.5% versus 76.8% (HR 0.63, 95% CI 0.48 to 0.82) in the pembrolizumab arm.4 KEYNOTE-522 evaluated pembrolizumab, an anti-PD-1 antibody, in combination with neoadjuvant chemotherapy followed by adjuvant pembrolizumab monotherapy for patients with high-risk early TNBC. This population typically faces a higher risk of recurrence and poorer prognosis compared to other breast cancer subtypes. The trial demonstrated a significant improvement in EFS, supporting the integration of immunotherapy into the treatment paradigm for this aggressive disease. Whether this EFS benefit translates into an overall survival advantage at longer follow-up is the outstanding question, and ASCO 2026 may be the venue where that answer emerges.

Underlying all of these trials is the ongoing methodological debate about pCR as a surrogate. A pooled analysis from the CTNeoBC consortium showed that pCR was prognostic at the individual patient level but that trial-level association between pCR improvement and long-term survival was inconsistent across subtypes, particularly in HR-positive disease.5 This has direct bearing on how regulators and guideline bodies should interpret neoadjuvant trial results, and ASCO 2026 presentations are likely to provoke that debate again. The CTNeoBC analysis highlighted the complexity of using pCR as a surrogate endpoint for long-term outcomes like overall survival or event-free survival, especially given the biological heterogeneity of breast cancer. While pCR is a strong prognostic marker for individual patients across most subtypes, its utility as a reliable surrogate endpoint for drug approval and policy decisions at the trial level remains contentious, particularly in HR-positive disease where the correlation is weaker. This ongoing discussion influences the design of future neoadjuvant trials and the interpretation of their results.

To delve deeper into the established principles of oncology, particularly relevant to understanding current breast cancer trials and their implications, we recommend the Oxford Handbook of Oncology.

CLINICAL IMPLICATIONS

The most immediate clinical consequence of ASCO 2026 data will fall on oncologists currently counselling HR-positive, node-positive patients about adjuvant CDK4/6 inhibition. If monarchE or NATALEE delivers an overall survival signal, the residual hesitancy around two years of abemaciclib or three years of ribociclib dissolves almost entirely. If the survival curves remain overlapping, the iDFS-versus-cost-and-toxicity calculation becomes much harder to resolve at the bedside, and NICE, ESMO, and NCCN will face pressure to either strengthen or qualify existing recommendations. Clinicians who have been deferring the conversation should not wait for the conference abstracts to brush up on the monarchE and NATALEE designs.

Patients with early TNBC and those navigating HER2-positive de-escalation decisions carry a different kind of uncertainty. For them, the appeal of avoiding months of additional therapy is real and reasonable, but the evidence base for biology-guided de-escalation remains built on surrogate endpoints in relatively small cohorts. The risk is that ASCO presentations will be framed optimistically in conference press releases before the full survival picture is clear, and patients will arrive in clinic having read headlines that outrun the data. That is not a hypothetical concern: it happened with neoadjuvant immunotherapy approvals where EFS was used as an accelerated approval endpoint before OS matured.

For Eli Lilly, Pfizer, Novartis, and Merck, the commercial stakes at ASCO 2026 are considerable. Adjuvant CDK4/6 inhibitors represent a large and still-growing market, and an OS readout in either direction will move prescribing behaviour faster than any label revision. Merck, in particular, needs the KEYNOTE-522 OS data to consolidate pembrolizumab's position in early TNBC against biosimilar and generics pressure on the chemotherapy backbone. The irony is that the trial most likely to produce a clean, interpretable result is also the one where the answer has been most anticipated for the longest time. ASCO 2026 may finally deliver it.

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REFERENCES

1. 1. Johnston SRD, Toi M, O'Shaughnessy J, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. Lancet Oncol. 2023;24(1):77-90. doi:10.1016/S1470-2045(22)00694-5
2. 2. Slamon DJ, Stroyakovskiy D, Yardley DA, et al. Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2- early breast cancer: primary results from the phase III NATALEE trial. J Clin Oncol. 2024;42(17):2040-2050. doi:10.1200/JCO.23.02852
3. 3. Llombart-Cussac A, Cortes J, Pare L, et al. HER2-enriched subtype as a predictor of pathological complete response following trastuzumab and lapatinib without chemotherapy in early-stage HER2-positive breast cancer (PHERGain): a randomised, open-label, phase 2 trial. Lancet Oncol. 2021;22(2):171-181. doi:10.1016/S1470-2045(20)30630-7

4. 4. Schmid P, Cortes J, Dent R, et al. Event-free survival with pembrolizumab in early triple-negative breast cancer. N Engl J Med. 2022;386(6):556-567. doi:10.1056/NEJMoa2112651

5. 5. Cortazar P, Zhang L, Untch M, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384(9938):164-172. doi:10.1016/S0140-6736(13)62422-8