The therapy of hormone receptor–positive (HR+) / HER2-negative (HER2−) breast cancer is dominated by endocrine therapy. In recent years, endocrine therapy has gained increasing significance, as shown by data from adjuvant SOFT and TEXT studies. The retrospective analysis of the HERA trial (Ahn SG et al., ESMO 2024, #233MO) presented at ESMO 2024, involving 965 premenopausal women, showed that the combination of an aromatase inhibitor (AI) and a GnRH analog (ovarian function suppression, OFS) was so effective that trastuzumab did not add meaningful efficacy, although all patients had HER2-positive tumors. In a comparison of Tamoxifen + OFS vs. aromatase inhibitor + OFS, the tamoxifen-containing regimen performed worse in overall survival after 10 years by 11.6%.

The effectiveness of anti-hormonal therapy was exploited by the IMPACT and later POETIC trials (Smith I et al., Lancet Oncol 2020), which demonstrated that a 2-week therapy with an aromatase inhibitor leading to Ki-67 reduction to <10% significantly reduced recurrence risk compared with patients without Ki-67 decline. The German ADAPT trial (Nitz U et al., JCO 2022) incorporated this effect into its design by combining the so-called dynamic Ki-67 with the Oncotype DX Recurrence Score (RS). The study showed that in patients with chemotherapy indication (cT1-4c, N0-1) who, after 4 weeks of endocrine induction therapy, exhibited Ki-67 ≤10% and an initial RS of 12–25, adjuvant endocrine therapy was sufficient. Contrary to the RxPONDER study, nodal-positive, premenopausal women did not derive chemotherapy benefit. It is important to note that the quality of endocrine induction therapy was decisive for response, i.e., Ki-67 decline. The greatest response was seen in premenopausal patients after induction therapy with an AI + OFS, while postmenopausal patients responded best to AI alone.

In ADAPTcycle, patients with intermediate risk after endocrine induction therapy were randomized to a chemotherapy-free arm with ribociclib (2 years) + AI (± OFS) versus a chemotherapy arm, to evaluate the value of endocrine-based versus chemotherapy strategies. The neoadjuvant-treated patient analysis was presented at ESMO Breast Cancer 2025 (Harbeck N et al., ESMO BC 2025) and, independent of nodal status, after 6–12 months showed no significant difference between endocrine-based therapy and chemotherapy in terms of pCR (ribociclib: 5.0% vs. chemotherapy: 7.7%, p=0.483). The VOG-01 study, presented at ASCO 2025 (Orlova R et al.), also showed that for premenopausal women, the combination of ribociclib + fulvestrant + OFS vs. chemotherapy achieved equivalent pCR and response rates with lower toxicity in the endocrine-based arm. Regarding the use of selective estrogen receptor degraders (SERDs), the coopERA study in the neoadjuvant setting of palbociclib + giredestrant or anastrozole demonstrated promising anti-proliferative and anti-tumor activity of the combination with giredestrant (Hurvitz S, Lancet Oncol 2023).
Additional neoadjuvant studies are bringing endocrine-based strategies with CDK4/6 inhibitors or PI3K inhibitors to the forefront, even in triple-positive (HR+/HER2+) early breast cancer, to increase response rates, lower recurrence, and enable personalized treatment planning. Examples include the TOUCH study (Malorni L et al., SABCS 2024, #RF1-02) presented at SABCS 2024 with palbociclib + letrozole versus Paclitaxel weekly, both with trastuzumab/pertuzumab and identical pCR rates; the GeparPiPPA trial (GBG 105) of the German Breast Group; the ongoing GeparPiPPA study evaluating the PI3K inhibitor inavolisib in HR+/HER2+ with PIK3CA mutation; and for the rare invasive lobular carcinoma, the phase II LOBSTER trial in HR+/HER2− early breast cancer examining neoadjuvant capivasertib in combination with

fulvestrant vs. fulvestrant alone.
Currently, targeted therapy is increasingly playing a role in neoadjuvant therapy for early breast cancer, and chemotherapy may become obsolete for a large proportion of HR+ patients - though this has not been proven yet.