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ESMO20 YO for YO: highlights on adjuvant CDK4/6 inhibitors in early hormone receptor-positive/HER2-negative breast cancer

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ESMO20 virtual conference brought us the results of two major randomized trials on the adjuvant use of cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) for early hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative breast cancer (BC). The two studies, PALLAS with palbociclib (ClinicalTrials.gov identifier NCT02513394) and monarchE with abemaciclib (NCT03155997), reported conflicting results. In the latter, adding abemaciclib for 2 years to standard endocrine therapy improved both the primary endpoint, invasive disease-free survival (DFS) with an absolute improvement of 3.5% at 2 years, as well as distant relapse-free survival (DRFS) with an absolute improvement of 3.3% at 2 years. In contrast, PALLAS reported that the addition of 2 years of adjuvant palbociclib did not affect either DFS or DRFS. Differences in the study populations could account for this discrepancy, although a subgroup analysis of PALLAS on high-risk patients matching the inclusion criteria of monarchE, approximately 58.7% of the entire patient population, did not demonstrate any benefit with palbociclib. In addition, rates of premature discontinuation due to adverse events were considerably higher with palbociclib, raising the question whether the results may be partly attributed to inadequate exposure to treatment. Crucially, longer follow-up is needed since HR+/HER2− BC has a protracted natural history.

However, this is only the beginning of the CDK4/6i saga in the early BC setting: results from the biomarker discovery TRANS-PALLAS program are eagerly awaited, as well as the results from the NATALEE trial on adjuvant ribociclib (NCT03701334). Other ongoing adjuvant studies utilize response to short-term neoadjuvant endocrine therapy for patient selection (NCT04055493, NCT04584853) or examine adjuvant CDK4/6i in other high-risk scenarios, such as resection of locally recurring BC (NCT03820830) or poor response to neoadjuvant chemotherapy (NCT01864746). Only time will clarify the role of these agents and the different compounds in the adjuvant setting.

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DISCLOSURE

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