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Management of ER+ HER2- mBC: Bringing Together Clinical & Real-World Evidence

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The combination of a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor and endocrine therapy (ET) has become a preferred first-line approach in the management of metastatic hormone receptor (HR)–positive/human epidermal growth factor receptor-2 overexpressing (HER2–) breast cancer (BC). The three available agents, palbociclib, abemaciclib, and ribociclib, all have uniformly demonstrated improvements in progression-free survival when added to ET. Whether these drugs prolong overall survival (OS) has been a topic of substantial study and discourse, with conflicting data coming from long-term follow-up of the initial randomized clinical trials as well as population-based analyses.

The interpretation of real-world studies may be limited by the lack of a comparator group, small sample size, short follow-up, and/or differences in outcome endpoint definitions. Only a few comparative effectiveness analyses of CDK4/6 inhibitor outcomes in MBC have been published to date, including DeMichele et al. (2021) using the Flatiron Health Analytic Database (Flatiron Health, New York, NY) and Ha et al. (2022) from one academic institution (Breast Medical Oncology database; MD Anderson Cancer Center, Houston, TX). Using the Flatiron Database, a comparative effectiveness real-world analysis demonstrated longer real-world PFS (rwPFS) and OS among all patients treated with palbociclib plus letrozole versus letrozole alone and among patients with at least one tumor response assessment. These analyses had a relatively small sample size and short follow-up time and were comparative with letrozole only. Therefore, additional research with both men and women, with an AI as the endocrine partner as per the CDK4/6 inhibitors label and with longer-term follow-up, is warranted to further evaluate these outcome findings in the real-world setting.

In clinical practice, patient populations and clinicians' treatment decisions differ from those in the controlled environment of a clinical trial. Such differences can potentially impact the effectiveness and safety of treatment. Observational real-world studies complement findings from clinical trials and provide important evidence demonstrating a therapy's efficacy and safety in more heterogeneous patient populations. An understanding of real-world treatment practices and patterns and how they impact the efficacy and tolerability of new drugs also provides important data that can guide clinicians on optimal drug dosing and subsequent indications and thus help improve routine clinical care. Such insight gained from real-world studies is reflected in the increasing use of real-world evidence in regulatory decision making.