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336P Everolimus in advanced breast cancer: A systematic review and meta-analysis

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Background: Everolimus (E) plus exemestane are approved for advanced hormone receptor (+) breast cancer (BC) after progression on non-steroidal aromatase inhibitors. The role of E is less well defined in other BC phenotypes and with other drugs. We conducted a systematic review and meta-analysis to assess the efficacy and safety of adding E to standard of care (SoC) in advanced BC regardless of tumor phenotype and treatment type.

Methods: The electronic databases PubMed and EMBASE, were searched for eligible randomized trials. Pooled hazard ratios (HR) for progression free survival (PFS) and overall survival (OS) and pooled risk ratios (RR) and odds ratios (OR) for objective response rates (ORR), clinical benefit rates (CBR) and grade 3 or higher toxicity were meta-analyzed using the generic inverse variance, the Mantel-Henszel and Peto method. To account for between-studies heterogeneity, random-effect models were used. Subgroup analyses compared survival outcomes by tumor phenotype.

Results: Data of 2,693 patients from 7 trials were analyzed. The addition of E to the SoC reduced the risk of disease progression by 33% (7 trials, HR 0.67, 95%CI 0.52-0.86). This did not translate into an OS benefit (4 trials, HR 0.91, 95%CI 0.62-1.33). In addition, E improved the ORR (6 trials, RR 0.91, 95%CI 0.85-0.97) and CBR (7 trials, RR 0.79 95%CI 0.65-0.97) while it increased the risk of developing $\geq$ grade 3 toxicity including stomatitis (OR 5.00, 95%CI 3.63-6.89) and pneumonitis (OR 3.13, 95%CI 1.83-5.36). The PFS benefit was more prominent for patients with hormone receptor (+) / HER2 (-) (HR 0.51, 95%CI 0.43-0.59) than HER2 (+) disease (HR 0.83, 95%CI 0.73-0.96; p for subgroup differences <0.001). For the HER2 (+) subgroup, the PFS benefit was restricted to hormone receptor (-) patients (HR 0.65, 95%CI 0.53-0.81 and HR 0.99, 95%CI 0.83-1.19 for hormone receptor (+) patients; p for subgroup differences 0.004).

Conclusions: E reduces the risk of disease progression in hormone receptor (+) advanced BC independent of endocrine therapy type. In HER2 (+) patients, the benefit is limited for hormone receptor (-) patients. Given the use of newer drugs in the first line, real-world data are needed to confirm whether the benefit persists for patients who develop resistance to CDK4/6 inhibitors.

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