

323P Endocrine therapy alone versus targeted combination strategy as first line treatment in elderly patients with hormone receptor-positive advanced breast cancer: Meta-analysis of phase II and III randomized clinical trials

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Background: Combined endocrine/targeted approaches have been investigated as first-line treatment in hormone receptors positive metastatic breast cancer (BC). Randomized trials showed that the addition of CDK (cyclin-dependent kinase) 4/6 inhibitors to endocrine therapy (ET) increase progression free survival (PFS). Elderly patients (aged >65 years) are under represented in most of the trials. Due to the multi-morbidity and the major toxicity associated with the targeted agents, the combination strategy in that subgroup is widely discussed. The present meta-analysis aimed to understand the role of the new endocrine approaches in elderly women.

Methods: This meta-analysis included first line phase II/III randomized published trials comparing ET to the experimental strategy. Trials with no data about hazard ratios (HR) for PFS in the subgroup of patients aged > 65 years were excluded. The heterogeneity of the data was evaluated by Chi-square Q test and I² statistic. Prospero registration number: CRD42019120215.

Results: 8 studies were included: 4 (Paloma1/TRIO-18, Paloma2, Monaleesa2, Monarch3) investigated the role of CDK 4/6 inhibitors, 2 trials (SWOG and FACT) analysed the combination of Fulvestrant plus Aromatase Inhibitors, while other two trials explored the association of ET with Bevacizumab (LEA) and Temozolomide (HORIZON), respectively. Overall, the meta-analysis showed a PFS advantage for the experimental arms [HR 0.77, p 0.016] with a significant high/moderate heterogeneity [I² 65.46%, p 0.005]. The 4 studies adding CDK4/6 inhibitors to ET showed a significant improvement in PFS compared to ET alone. No significant advantages for the addition of anti-angiogenic agents or Fulvestrant to ET have been found.

Conclusions: The novel experimental strategies showed an improvement in PFS in elderly patients. Adding CDK4/6 inhibitors to ET significantly prolongs PFS as compared to ET alone, the magnitude of PFS benefit is age-independent. To define the role of novel agents, future trials should be designed taking in account not only the age, but also adequate geriatric assessment and comorbidity status.

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