Volume 20, Issue 10, October 2019, Pages 1360-1369

Articles

Endocrine treatment versus chemotherapy in postmenopausal women with hormone receptor-positive, HER2-negative, metastatic breast cancer: a systematic review and network meta-analysis

MarioGiulianoMD[ab†]FrancescoSchettiniMD[aco†]CarlaRognoniPhD[d]ManuelaMilaniMD[e]ProfGuyJerusalemMD[f]ThomasBachelotMD[g]MichelinoDe LaurentiisMD[h]GuglielmoThomasMD[i]PietroDePlacidoMD[a]GraziaArpinoMD[a]ProfSabinoDePlacidoMD[a]MassimoCristofanilliMD[j]AntonioGiordanoMD[k]FabioPuglisiMD[lm]BarbaraPistilliMD[n]AleixPratMD[cop]LuciaDel MastroMD[qr]SergioVenturiniPhD[ds]DanieleGeneraliMD[et]

Summary

Background

Although international guidelines support the administration of hormone therapies with or without targeted therapies in postmenopausal women with hormone-receptor-positive, HER2-negative metastatic breast cancer, upfront use of chemotherapy remains common even in the absence of visceral crisis. Because first-line or second-line treatments, or both, based on chemotherapy and on hormone therapy have been scarcely investigated in head-to-head randomised controlled trials, we aimed to compare these two different approaches.

Methods

We did a systematic review and network meta-analysis with a systematic literature search on PubMed, Embase, Cochrane Central Register of Clinical Trials, Web of Science, and online archives of the most relevant international oncology conferences. We included all phase 2 and 3 randomised controlled trials

investigating chemotherapy with or without targeted therapies and hormone therapies with or without targeted therapies as first-line or second-line treatments, or both, in postmenopausal women with hormone-receptor-positive, HER2-negative metastatic breast cancer, published between Jan 1, 2000, and Dec 31, 2017. Additional recently published randomised controlled trials relevant to the topic were also subsequently added. No language restrictions were adopted for our search. A Bayesian network meta-analysis was done to compare hazard ratios (HRs) for progression-free survival (the primary outcome), and to compare odds ratios (ORs) for the proportion of patients achieving an overall response (the secondary outcome). All treatments were compared to anastrozole and to palbociclib plus letrozole. This study is registered in the Open Science Framework online public database, registration DOI 10.17605/OSF.IO/496VR.

Findings

We identified 2689 published results and 140 studies (comprising 50 029 patients) were included in the analysis. Palbociclib plus letrozole (HR 0·42; 95% credible interval [CrI] 0·25–0·70), ribociclib plus letrozole (0·43; 0·24–0·77), abemaciclib plus anastrozole or letrozole (0·42; 0·23–0·76), palbociclib plus fulvestrant (0·37; 0·23–0·59), ribociclib plus fulvestrant (0·48; 0·31–0·74), abemaciclib plus fulvestrant (0·44; 0·28–0·70), everolimus plus exemestane (0·42; 0·28–0·67), and, in patients with a *PIK3CA* mutation, alpelisib plus fulvestrant (0·39; 0·22–0·66), and several chemotherapy-based regimens, including anthracycline and taxane-containing regimens, were associated with better progression-free survival than was anastrozole alone. No chemotherapy or hormone therapy regimen was significantly better than palbociclib plus letrozole for progression-free survival. Paclitaxel plus bevacizumab was the only clinically relevant regimen that was significantly better than palbociclib plus letrozole in terms of the proportion of patients achieving an overall response (OR 8·95; 95% CrI 1·03–76·92).

Interpretation

In the first-line or second-line setting, CDK4/6 inhibitors plus hormone therapies are better than standard hormone therapies in terms of progression-free survival. Moreover, no chemotherapy regimen with or without targeted therapy is significantly better than CDK4/6 inhibitors plus hormone therapies in terms of progression-free survival. Our data support treatment guideline recommendations involving the new combinations of hormone therapies plus targeted therapies as first-line or second-line treatments, or in both settings, in women with hormone-receptor-positive, HER2-negative metastatic breast cancer.