Concurrent and sequential initiation of ovarian function suppression with chemotherapy in premenopausal women with endocrine-responsive early breast cancer: an exploratory analysis of TEXT and SOFT


Background
Recent breast cancer treatment guidelines recommend that higher-risk premenopausal patients should receive ovarian function suppression (OFS) as part of adjuvant endocrine therapy. If chemotherapy is also given, it is uncertain whether to select concurrent or sequential OFS initiation.

Design and methods
We analyzed 1872 patients enrolled in the randomized phase III TEXT and SOFT trials who received adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer and upon randomization to an OFS-containing adjuvant endocrine therapy, initiated gonadotropin-releasing-hormone-agonist triptorelin. Breast cancer-free interval (BCFI) was compared between patients who received OFS concurrently with chemotherapy in TEXT (n = 1242) versus sequentially post-chemotherapy in SOFT (n = 630). Because timing of trial enrollment relative to adjuvant chemotherapy differed, we implemented landmark analysis re-defining BCFI beginning 1 year after final dose of chemotherapy (median, 15.5 and 8.1 months from enrollment to landmark in TEXT and SOFT, respectively). As a non-randomized treatment comparison, we implemented comparative-effectiveness propensity score methodology with weighted Cox modeling.

Results
Distributions of several clinico-pathologic characteristics differed between groups. Patients who were premenopausal post-chemotherapy in SOFT were younger on average. The median duration of adjuvant chemotherapy was 18 weeks in both groups. There were 231 (12%) BC events after post-landmark median follow-up of about 5 years. Concurrent use of triptorelin with chemotherapy was not associated with a significant difference in post-landmark BCFI compared with sequential triptorelin post-chemotherapy, either in the
overall population (HR = 1.11, 95% CI 0.72-1.72; P = 0.72; 4-year BCFI 89% in both groups), or in the subgroup of 692 women <40 years at diagnosis (HR = 1.13, 95% CI 0.69-1.84) who are less likely to develop chemotherapy-induced amenorrhea.

Conclusion
Based on comparative-effectiveness modeling of TEXT and SOFT after about 5 years median follow-up, with limited statistical power especially for the subgroup <40 years, neither detrimental nor beneficial effect of concurrent administration of OFS with chemotherapy on the efficacy of adjuvant therapy that includes chemotherapy was detected.

Clinicaltrials.gov
NCT00066690 and NCT00066703.