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LATEST ONCOLOGY UPDATES

Title:
Five Years of Letrozole Compared with Tamoxifen as Initial Adjuvant Therapy for Postmenopausal Women with Endocrine-Responsive Early Breast Cancer: Update of Study BIG 1-98

Study Design
BIG 1.98 is a four arm trial evaluating aromatase inhibitors for post-menopausal hormone receptor positive breast cancer. Subjects 8,028) were randomized to receive either:

ARM A: tamoxifen alone for five years
ARM B: letrozole alone for five years
ARM C: tamoxifen followed by letrozole to complete 5 years of treatment
ARM D: letrozole followed by tamoxifen to complete 5 years of treatment

The previous 26 month report evaluated ARM A and ARM B as well patients on ARM C and D up to the point of switching to the different agent.

The current 51 month analysis published in this manuscript is only presenting results for subjects on ARM A and B (4922 subjects).

Study Question
Is letrozole superior to tamoxifen with respect to DFS.

Results
Letrozole is superior to tamoxifen with respect to DFS. There is no statistical significant difference between the two arms for OS. According to this publication - patients on tamoxifen experienced more thromboembolic events, endometrial pathology, hot flashes, night sweats, and vaginal bleeding. Patients on letrozole experienced more bone fractures, arthralgia, low-grade hypercholesterolemia, and cardiovascular events other than ischemia and cardiac failure

Author Conclusions
The present updated analysis, which was limited to patients on monotherapy arms in BIG 1-98, yields results similar to those from the previous primary analysis but more directly comparable with results from other trials of continuous therapy using a single endocrine agent.

Study Commentary

- It is again important to note that the results presented here focused just on Arms A and B and we don't have any additional information on the switch arms.
- With now f/up time of 51 months, there was no new safety concerns noted as compared with the previous 26 month follow up
- Hypercholestolemia: Subjects on letrozole did document hypercholesterolemia when compared to those on tamoxifen. However, when subjects were compared to baseline there was no additional hypercholesterolemia seen indicating this difference is likely due to cholesterol lowering effects of tamoxifen. Also in the only placebo controlled trial in this population (MA.17), patients on letrozole did not have hypercholesterolemia or an increase in cardiac events.

Bottom line for Canadian Oncology professionals

Letrozole is superior to tamoxifen in the treatment of post-menopausal hormone receptor positive early stage breast cancer. There appears to be no new safety concerns with longer follow up of 51 months. The results seen in this trial are comparable to those seen in the ATAC trial. In the clinical setting we now have two aromatase inhibitors that have shown to be superior to tamoxifen: Anastrazole and Letrozole. We still don't have data to suggest if one AI is superior to another or what is the optimal endocrine strategy i.e. upfront vs. sequential vs. extended. Ongoing trials (FACE: Letrozole vs. Anastrozole; MA. 27 Exemestane vs. Anastrazole) and the final report on the BIG 1.98 four arm trial will address these questions.